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LEARNED CONTROL OF CORONARY BLOOD FLOW

DISSERTATION

Presented in Partial Fulfillment of the Requirements for
the Degree Doctor of Philosophy in the Graduate
School of the Ohio State University

By

Frederick Alan Ernst, B.S., M.A.

* * * * *

The Ohio State University

1976

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To Star, Brian, Brenda, Mom & Dad

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Because of its intimate involvement in the most common variety of heart disease, coronary circulation deservedly has received a great deal of attention from cardiologists and cardiovascular physiologists. (Gregg & Fisher, 1963; Gregg, 1959; Gorlin, 1971, 1974; Sabiston, 1974). However, in spite of the fact that psychologists in recent years have demonstrated a parallel interest in cardiovascular psychophysiology, (Black, 1965; Black & DeToledo, 1968; Black, 1971; Miller, & Weiss, 1969; Miller, 1969; Obrist, Black, Brever and DiCara, 1974; Harris & Brady, 1974), coronary circulation has been virtually ignored in their efforts.

Over a decade ago the influence of simple aversive environmental events on coronary circulation were examined in Gregg's cardiology laboratory (Rayford, Kauri, & Gregg, 1965) but, because of its primary focus on hemodynamic interrelationships, the study did not attend as carefully to the measurement, definition, and manipulation of the events in question. Later an extension of this work was examined in Europe where an aversive Pavlovian conditioning paradigm was employed to study the effects of "anxiety" on cardiovascular events including coronary circulation, but once again, careful selection and precise measurement of the environmental parameters seemed somewhat blurred so that a meaningful psychological interpretation of their results is consequently difficult (Bergamaschi, Caravaggi,

Mandelli & Shanks, 1973; Miller, 1969).

During this same period psychologists had become intensely involved in examining cardiovascular activity with aversive respondent conditioning procedures and were awakening to the possibility that cardiovascular and other visceral behaviors were equally responsive to operant conditioning. These two conditioning paradigms are accepted by psychologists as the basis for most if not all learning.

There are a great number of studies available on the aversive respondent conditioning of cardiovascular function in animals and significantly fewer on operant control, much less aversive operant control, of cardiovascular function with infrahuman species. Following is an examination of the literature on respondent and operant conditioning respectively with a primary emphasis on the operant paradigm (See Appendix C for a comprehensive review and analysis of the respondent conditioning literature).

PIONEERING ANIMAL STUDIES

RESPONDENT CONDITIONING

Aversive respondent conditioning of various autonomic functions has been the subject of considerable research interest in recent years. Within this area, cardiovascular functions have been the most popular focal measures. Ironically, in spite of this interest and activity, Harris & Brady (1974) recently concluded that the reports "appear to justify few generalizations about the classical

conditioning of autonomic responses and contribute more to the complexity of the process than to its clarification". While their assertion seems valid for most of the work in this general area, there does appear to be a reasonable degree of consistency in findings relative to conditioned heart rate (HR) changes in the context of the aversive respondent paradigm for most infrahuman laboratory species.

In fact a careful examination of the literature on HR conditioning with infrahuman subjects indicates rather unequivocally that deceleratory CRs are common to fish (Otis, et.al., 1957; Offutt, 1971; Scobie, 1973), lobsters (Offutt, 1970), rabbit (Schneiderman, et.al., 1974), rat (Holdstock & Schwartzbaum, 1965; Parrish, 1967; Tighe, et.al., 1968; Phillips & Martin, 1972) and cat (Bruner, 1969; Hein, 1969; Howard, et.al., 1974; Howard, et.al., 1975), while acceleratory CRs have been well established for pigeons (Cohen & Durkovic, 1966; Durkovic & Cohen, 1969a, 1969b; Cohen, 1974), monkeys (Smith & Stebbins, 1965; Ramsay, 1970; Schneiderman, et.al., 1975; Randall, et.al., 1975), and dogs (Dykman, et.al., 1956; Fitzgerald, 1966; Pare, 1967; Lynch, 1968; Obrist, et.al., 1972). Why some species show consistent cardioacceleratory CRs while others manifest cardiodeceleration is not clearly understood. Indeed a simple neurophysiological explanation cannot adequately account for clearly opposite results. However, it is suggested here that the direction of the

conditioned HR change can partially be accounted for in the basis of species-specific defense reactions (SSDR) similar to what has been proposed by Bolles (1970). More specifically, it seems evident that conditioned HR deceleration is common to animals for whom "freezing" is frequently observed as an SSDR (e.g., cat, rat, and rabbit), and conditioned HR acceleration is peculiar to animals in whom spontaneous "flight" is the more common SSDR (e.g., pigeon, dog, and monkey). The decelerative HR can be said to anticipate the decreased muscle activity of "freezing" and the accelerative HR to anticipate the increased muscle activity of immediate or spontaneous escape. In any event, these propositions seem clearly testable under both laboratory and "natural" circumstances.

Other cardiovascular dynamics have not received as much research attention as HR. Conditioned blood pressure (BP) increases have been demonstrated for the rabbit (Yehle, et.al., 1967; Schneiderman, et.al., 1969), monkey (Ferreira, et.al., 1969; Schneiderman, et.al., 1975; Randall, et.al., 1975; Klose, et.al., 1975) and dog (Newton, 1967; Perez-cruet & Gaertner, 1967; Kakigi, 1971; Obrist, et.al., 1972) with only one exception (Antal & Gantt, 1970). The exception, however, is one of very few studies in which the trace paradigm was employed with a focus on carotid BP possibly accounting for this discrepancy. Hein (1969) demonstrated conditioned BP decreases in cats which is the

only study of its kind with this particular species.

Conditioned blood flow (BF) changes have been examined systematically in only a few studies. Antal & Gantt (1970) demonstrated increases in blood flow in the femoral artery perfusing the leg to which shock was administered in a leg flexion study. Smith & Stebbins (1965) found conditioned increases in central aortic BF concomitant with HR acceleration to an aversive CS.

In a study of particular relevance to the present investigation Bergamaschi, Caravaggi, Mandelli, and Shanks (1973a) demonstrated significant increases in left circumflex coronary flow as a UCR to the firing of a gun. Concomitant increases in HR, cardiac output, and left ventricular work with decreases in peripheral and coronary resistances were also found. Interestingly, no significant change in aortic pressure was reported. When the gun firing was preceded by a tone, rapid acquisition of anticipatory increases in coronary flow was found to occur with HR deceleration and central aortic blood pressure increases (Bergamaschi, Caravaggi, Mandelli, & Shanks, 1973b). Presumably the baroreceptor system would seem responsible for this latter finding. These effects were augmented by sympathetic beta-adrenergic blockade. It should be mentioned that only three dogs were used in the study and they were not immobilized by neuromuscular blocking agents.

Another study related to the present investigation which merits consideration is an anecdotal report (Newton & Ehrlich, 1969) who described coronary vasodilation in dogs who were exposed to a sudden entrance of people into an experimental room in which the animals had been treated. They were unable to determine specifically whether the response was an unconditioned "effect of person" or whether the person acquired properties of a potential UCS by occluding the animals' coronary artery subsequent to each entrance of the room.

OPERANT CONDITIONING

Undoubtedly the most significant work in operant conditioning was that of Miller (1969) and his colleagues (DiCara, 1970; DiCara & Miller, 1968a; DiCara & Miller 1967; DiCara & Miller, 1968b). Using surarized rats Miller was able to bring a wide variety of diverse autonomically-mediated visceral and glandular responses under operant control. In so doing, he helped destroy convictions among physiologists and psychologists (cf., Kimble, 1961) that the autonomic nervous system was "vegetative" in character and therefore not responsive to the laws of operant conditioning.

The earliest work in his laboratory (Miller & Carmona, 1967), focused on the control of salivation in thirsty dogs through the use of water as a reinforcing stimulus. Since he was able to reward increases and decreases in

salivation, a respondent conditioning artifact was ruled out. However, because of the possibility that these responses might have been mediated or indirectly affected by skeletal responses, later work was carried out with animals fully paralyzed by curare and the locus of reinforcement was shifted to the rewarding areas of the brain by electrical stimulation (ESB). In this study, Trowill (1967) was able to condition systematic increases and decreases in heart rate, and moreover, to bring these changes under discriminative operant control. Later DiCara and Miller (1968) were able to produce even more dramatic changes utilizing the escape-avoidance paradigm to shape cardiovascular changes.

Intrigued by these discoveries, Miller & Banuazizi, (1968) pursued questions relating to the range and specificity of the phenomena. In their experiment both heart rate and intestinal contractions were manipulated independently but simultaneously. These results encouraged DiCara and Miller (1967) to attempt an almost incredible control of urine formation in the kidney, and in their success, corresponding effects on glomerular filtration, renal blood flow, and osmolarity were discovered.

Having further expanded the already remarkable range of functions they controlled and after successfully demonstrating comparable results with peripheral vasomotor responses (DiCara & Miller, 1968a; Pappas, DiCara, &

Miller, 1970; DiCara & Miller, 1968b) DiCara & Miller (1968c) produced increased vasodilation in the ear of one rat while relative vasoconstriction in the other ear of the same animal was successfully acquired. No corresponding changes were noticed in opposite pairs of paws further underscoring the truly remarkable degree of specificity. In a further demonstration of specificity involving regional blood flow, Carmona, Miller, & Demierre (1974) demonstrated operant control of perfusion in the gastric wall of curarized rats independent of otherwise related cardiovascular dynamics.

Although these studies have been difficult to replicate (Miller & Dworkin, 1974; Carmona, Miller, & Demierre, 1974), problems of replication seem peculiar to Miller's laboratory. Several reports from other laboratories have confirmed the basic tenets of Miller's position, especially those studies in which heart rate was the target of operant control.

REPLICATIONS: HEART RATE

Black (1968) was the first to investigate operant conditioning of heart rate in curarized dogs. In a brief report, he claimed bi-directional aversive control in which deceleration was the most difficult to achieve. The difficulty in shaping operant decreases in heart rate (HR) is not surprising in light of two considerations: a) the curare preparation is known to have vagal-inhibitory

effects thereby elevating basal HR (Howard, Gaebeline, Galosy, & Obrist, 1975), and b) the respondent CR in the aversive paradigm is cardioacceleration for dogs (Cohen & Obrist, 1975) which can reciprocally inhibit the target responses when operant decelerations are attempted. Black's report stands as the only one of its kind in which a cardiovascular behavior was operantly modified in dogs.

The earliest study outside Miller's lab in which operant conditioning of HR in rats was investigated is that of Hothersall & Brener (1969). Increases and decreases in HR were shaped by electrical stimulation of the brain (ESB) which was signalled by a visual discriminative stimulus. After an adaptation period of CS-only trials, six curarized rats were taught to increase HR for ESB and six were taught to decrease HR for the same reward. Each group was also subjected to extinction trials in each of four sessions. The magnitude of the acquired response for each group improved across sessions.

Curarized rats were also the subjects of Slaughter, Hahn, & Rinaldi (1970) who employed a similar discriminative shaping program. Ten animals were taught to increase HR and ten to decrease HR for ESB after having been pre-trained to bar-press for ESB. Varying amounts of pre-training did not selectively affect subsequent HR performance. The acceleratory group averaged 14% increases in HR while the deceleratory group averaged 9% decreases.

DiCara & Stone (1970) examined concentrations of brain and cardiac catecholamines during operant HR conditioning of curarized rats. A compound discriminative stimulus signalled ESB for 44 rats divided equally into two groups: cardioacceleration and cardiodeceleration. Modest changes of 9% and 8% were conditioned respectively while cardioacceleratory rats were found to have significant increases in endogenous brain and cardiac catecholamines following conditioning.

Fields (1970) examined conditioning of specific features of the cardiac cycle in rats who were immobilized by curare. Although he reports using 46 subjects, almost all of his data are presented in a single-subject format. Punishment with shock and ESB reward were both used to shape increases and decreases in PR and PP intervals (See appendix for further details on cardiovascular physiology). His major finding was that PR and PP intervals could be selectively increased or decreased independent of changes in the RR interval. Presumably sino-atrial conduction (and therefore atrial contraction) was thus selectively increased and decreased without corresponding changes in atrio-ventricular conduction (and ventricular contraction). This would suggest a highly specific neuro-cardiac control system which can selectively affect atrial versus ventricular electrical function.

Goesling & Brener (1972) employed shock in an avoidance paradigm with curarized rats trained to increase and decrease HR. Prior to HR conditioning rats were trained to be immobile. Those with pre-training in immobilization showed greater HR decrements during conditioning of decreases than those without pre-training.

In another aversive conditioning study, DiCara, Braun, & Pappas (1970) investigated HR conditionability in neocorticate versus normal rats. Neither increases nor decreases were acquired by neocorticates while normals showed a significant relative difference between acceleratory and deceleratory sub-groups. Interestingly, however, the magnitude of decreases across segments of conditioning was significant while for increases it was not. Since the aversive respondent CR in rats is cardiodeceleration, it would be difficult to argue that operant conditioning was ever achieved in the study.

In a more recent investigation, Roberts, Lacroix, & Wright (1974) reported dramatic HR deceleration in curarized rats who were punished for rates beyond a specified level. The decelerative response was highly resistant to extinction. However, since the punishing shock was un-signalled the issue of extinction is made somewhat ambiguous. Interestingly operantly induced HR acceleration was found to be much more difficult to condition and, in fact, possible in only three of ten animals. The remaining

seven rats actually learned deceleration in spite of the fact that such responses were consistently punished. Clearly, this is not a surprising finding in light of the observation that anticipatory and unconditioned cardiac responses to punishment are patently deceleratory in the rat (Cohen & Obrist, 1975; See also, Appendix A).

Most recently, Cabanac & Serres (1976) ingeniously employed a peripheral heat reward to modify HR in curarized rats. Subjects were tested in a chamber with double walls between which ice was packed to create a surrounding cold. An overhead 250 w infrared lamp was triggered to provide heat reinforcement for HR increases in one group of rats and HR decreases in another group. Pre-testing the effects of various changes in body temperature on heart rate generated a linear regression which allowed the investigators to systematically examine the influence of the contingency per se by subtracting the empirically determined unconditioned change in HR produced by the temperature manipulation from the rewarded change in HR. Small but highly consistent increases and decreases in HR were found for all but one rat in each of the rewarded groups.

The remaining studies in which HR was modified by operant conditioning are from Engel's laboratory with rhesus monkeys. Typically, immobilization of primates in conditioning studies is accomplished by a restraint chair rather than the curare preparation so often used with other

laboratory subjects. In Engel's experiments monkeys are chronically prepared in a primate chair and allowed to adapt to the immobilization for periods of up to several months. Engel & Gottlieb (1970) employed this procedure with an avoidance conditioning paradigm to train three rhesus monkeys to increase and decrease their heart rates in varying sequences. One animal learned to increase and then decrease HR to two respective discriminative stimuli and two others learned the same responses in reverse order. Blood pressure was highly correlated with HR in a positive direction during HR deceleration but not during acceleration. The differences between systolic pressures during deceleration and acceleration were not significant. The same was true for diastolic pressures. This would suggest, as the investigators note, that HR changes were not mediated by pressor reflexes such as the baroreceptor feedback loop.

In a later study Engel (1974) used an identical dual discriminative avoidance procedure to train four restrained rhesus monkeys in HR speeding and slowing. Blood pressure was again monitored to investigate potential vasomotor mediation of HR conditioning. Also EEG was monitored to explore changes affected by behavioral or cortical arousal. All animals acquired reliable increases and decreases in HR but their performance seemed to deteriorate in late training sessions. In this study highly significant positive

correlations were found between HR and blood pressure for both speeding and slowing. The correlations increased with training for slowing and remained approximately the same for speeding. Correlations for HR with percentage time of high voltage in the 8-14 Hz band of the EEG were negative for speeding and slowing in both early and late phases of training.

Ainslie & Engel (1975) extended the same avoidance paradigm by examining the respondent CR to a warning signal and the response to a combined respondent CS and operant avoidance signal. The anticipatory CR in an aversive respondent paradigm for primates is HR acceleration. However, when monkeys were taught to slow their HR to a visual avoidance cue and the cue was combined with an auditory respondent CS previously eliciting acceleration, the net effect was a predominance of the operant response. However, the previously conditioned increase in blood pressure was not suppressed by the avoidance cue in spite of the fact that HR was. This study serves as an excellent example of the power of the operant conditioning paradigm and the fascinating potential for specificity in the cardiovascular control system.

These studies provide strong confirmation of the notion that HR can be controlled with operant conditioning procedures. Conditioning of HR has been convincingly demonstrated in several species and several laboratories in

which more than one paradigm has been employed. The same can not be asserted for operant conditioning of vasomotor function.

REPLICATIONS: VASOMOTOR FUNCTION

As mentioned above, among the wide variety of visceral and glandular behaviors which were demonstrated by Miller and his students to be manipulable by operant conditioning, peripheral vasomotor responses were shown to be capable of the most remarkable specificity. DiCara & Miller (1968a) trained curarized rats to avoid shock by emitting increases and decreases in systolic blood pressure of 22.3% and 19.2% respectively. Moreover these responses did not correlate with heart rate or anal temperature during any phase of the training.

In an extension and replication of the previous study, Pappas, DiCara, & Miller (1970) trained non-curarized free-moving rats to increase or decrease systolic blood pressure to escape from or avoid shock. The group rewarded for increases averaged 28.4 mm/Hg of absolute change while those rewarded for decreases achieved a mean absolute change of 15.1 mm/Hg. Interestingly, when subjects were tested for retention under curare absolute changes in both directions diminished to slightly more than 10 mm/Hg. Correlations with HR were not significant in either case.

No other attempts to replicate operant conditioning of blood pressure in curarized rats have been reported from

Miller's or any other laboratory. Only two infrahuman studies have since attempted operant modification of blood pressure in another laboratory and both used non-curarized primates as subjects. Plumlee (1969) conditioned increases in diastolic blood pressure of up to 60 mm/Hg in rhesus monkeys who avoided shock by maintaining criterion diastolic increases for a 1-sec. period. All of the four monkeys responded to the avoidance paradigm and a fifth subject who was yoked to one of the experimental animals showed no elevations to the warning signal but normal elevations to shock. This is a surprising result for the yoked control since conditioned elevation in blood pressure during aversive respondent conditioning is a well-documented finding for primates (Cohen & Obrist, 1975).

Harris, Findley, & Brady (1971) combined a shock-avoidance and food-reward procedures to train two baboons to emit increases in diastolic blood pressure of 50-60 mm/Hg. Heart rate changes were variable and only rarely were they systematically related to achieved blood pressure changes. Furthermore the investigators reported no observation of significant changes in posture or respiration which might have systematically affected the acquired blood pressure response.

Neither the Plumlee nor Harris, et.al. study attempted to shape decreases in blood pressure. Clearly then, their results must be interpreted with the understanding that the

respondent characteristics of their procedures might well have accounted for a proportion of the response they presumably modified by operant conditioning.

To date, Miller and his students are the only investigators to report operant conditioning of regional blood flow in laboratory animals. There is no evidence in the literature that anyone has even attempted to replicate the studies in which blood flow was controlled to the ears, gastric wall, and kidneys of curarized rats or, for that matter, any other species. For this reason, alone, an attempt to replicate these studies would seem warranted and important. (Table 1 summarizes the characteristics and results of the operant conditioning studies).

REGIONAL BLOOD FLOW: CORONARY CIRCULATION

In light of the basic and clinical interest in the control of regional blood flow, an obvious yet unexplored area would appear to present itself with potential clinical ramifications of a most profound nature, namely, coronary circulation. The coronary arteries are richly innervated by both sympathetic and parasympathetic branches of the autonomic nervous system (Milnor, 1974) quantitatively unsurpassed by any other arterial system in the body (Ruch & Fulton, 1960). In fact, Gorlin (1974) points out that the coronary system is estimated to be capable of dilation "to a degree sufficient to increase coronary flow five times without changes in any other mechanical supply factor

(p.110)." Since the tonic state of the coronaries is a slight degree of constriction (Milnor, 1974) the potential for commensurate independent decreases in coronary blood flow would seem important from both a basic and a clinical standpoint. Of course, the clinical importance of achieving operant control of increases in coronary flow should be obvious.

Indeed myocardial infarction and angina pectoris are clearly disorders of insufficient blood flow. However, in spite of the fact that these types of ischemic heart disease cause more deaths than any other disease, virtually no systematic attention has been afforded this important problem of blood flow by psychologists interested in visceral learning and biofeedback. Although atherosclerotic disease is the most frequent cause of inadequate coronary blood flow, a significant frequency of angina pectoris and myocardial infarction has been observed in the absence of any atherosclerotic obstruction (Roberts, 1972; Edwards, 1969; Hackel, et.al., 1969). A syndrome known to cardiologists as Prinzmetal's variant angina pectoris is frequently observed in patients in whom angiography reveals little or no coronary obstruction while blood flow is partially or completely blocked by arterial spasm. Japanese scientists (Endo, et.al., 1976; Yasue, et.al., 1974) have recently documented the autonomic role in this disorder by inducing spasms and ischemia with associated ECG changes by

injections of parasympathomimetic agents (methacholine and pilocarpine) in patients with the Printzmetal syndrome. This autonomic influence is therefore fully recognized if not completely understood.

Pilot work from this laboratory has already demonstrated that the coronary vasculature is highly responsive to the aversive respondent conditioning paradigm. Dramatic increases in coronary blood flow were elicited by shock and commensurate increases were formed to a tone which preceded shock (See pg. v for references to this work). Also, early attempts to modify coronary blood flow by operant procedures indicated that large increases in flow could be shaped to increase further and that response latencies to a fixed-criterion increase improved with practice (See Appendix A). However, it is difficult to determine the unfounded influence of operant contingencies on increases in coronary flow when the escape-avoidance paradigm is employed since the respondent characteristics of this paradigm so dramatically affect the response in the target direction. For this reason, the present study focuses on the aversive operant control of coronary decreases primarily. If operant decreases in coronary blood flow can be readily shaped by escape-avoidance contingencies, then respondent conditioning artifacts can be ruled out.

The major hypothesis of the present proposal is that the coronary circulation is a bi-directional response

which obeys the laws of operant conditioning in the context of the escape-avoidance paradigm.

METHOD

Subjects. Fifteen mongrel dogs ranging in weight from 25-60 lbs. were used in the present study.

Apparatus. The primary apparatus was an Astrodata physiological monitor with a Honeywell 1508 Visicorder for light-sensitive recordings. Mean and pulsatile aortic and coronary blood flow were monitored through Statham electromagnetic flow probes. Heart rate ECG was measured through electrodes situated at contralateral limbs of the animal and central aortic blood pressure was monitored by a catheter positioned in the left femoral artery the tip of which was situated in the descending portion of the aortic arch. The catheter was connected to a Statham P-23-DB pressure transducer. A Harvard respirator was used during open-chest surgery and during the conditioning procedure during which the subject was immobilized by succinylcholine chloride (Anectine). Monophonic headphones delivered a 1000-Hz tone and a shock stimulator delivered an 8 m.a. shock to the animal's left hindleg via two electrode plates (3 cm X 3 cm). Scheduling and programming of the tone (CS), shock (UCS), and operant contingencies were controlled by an Aardvark Electronics Sandbox I event programmer.

Surgical Procedure. Following the procedure of Kezdi, et.al. (196-) dogs were anesthetized with pentobarbital sodium (30 mg/kg) and an intratracheal catheter was secured to regulate and maintain breathing by a Harvard respirator. The left chest was opened through the fourth intercostal space extending from the sternum to the mid-axillary line. Vertical retraction allowed full exposure of the heart and great vessels. The pericardial sac was incised and the edges sutured to the chest wall. The ascending aorta was then dissected from the surrounding connective tissue sheath and its circumference was determined for flow probe fit. A statham magnetic flow probe was selected and situated around the aorta allowing for a maximum constriction of 5 to 10%.

The left atrial appendage was then retracted and the left circumflex coronary artery was dissected from surrounding tissue. A statham magnetic flow probe was selected and secured around the artery once again allowing for a maximum of 5 to 10% constriction.

The coronary probe wire was brought through an opening made about one cm lateral to the pericardial incision and the aortic probe wires were sutured at the end of the pericardial incision. Using 1 to 0 catgut, the ribs were brought together and bound at several points. After the lungs were fully inflated, the chest was sealed with the last tie in the muscle layer. Openings were made 10 to 15

cms lateral to the final skin closure and the wires were brought through at this point. The animal was then bandaged securely around the chest and placed in recovery with a heating blanket.

Prior to experimentation subjects were allowed to recover from surgery (usually 4 - 7 days) during which rectal temperature, white blood count, and hematocrit were monitored.

Experimental Procedure. Each animal was tested individually by being placed and secured on a surgery table immediately after which succinylcholine (0.2 mg/kg/hr) was administered intravenously. Upon respiratory arrest, the S was respirated mechanically at a rate of 10-18 cycles per minute with an inspiration/expiration ratio of 1:1. The connector ends of the implanted flow probes were then connected via cables to Statham flow meters the output of which was directed to a Tetronex oscilloscope and Honeywell Visicorder via the Astrodata amplifying system. The audio headphones were then secured to the animal's head by adhesive tape after which the two shock electrodes were positioned at a shaven area of the S's left hindleg with an electrode paste medium. The blood pressure catheter and ECG electrodes were then situated and the S was allowed to acclimate to the setting during which electrical calibration for the various measures were adjusted. Prior to the initiation of the experiment, the S's eyes were covered by

a cloth towel and a white noise was begun through the headphones. Where possible, four cardiovascular measures were continuously monitored during the conditioning session: mean coronary blood flow, mean aortic blood flow, heart rate ECG, and mean central aortic blood pressure.

Respondent Conditioning Procedure. After the acclimation period, the CS was presented alone for a 30-second period several times spaced by a 4-minute mean variable intertrial interval. Physiological recordings were taken during the CS presentation and during 30-second pre-CS and post-CS periods. This phase of the experiment was designed to assess the course of habituation to the CS.

After habituation the CS was then consistently followed by an overlapping 10-second UCS after which both were terminated simultaneously. Ten such acquisition trials were presented during which physiological readings were obtained including pre-CS-UCS and post-CS-UCS periods. Following acquisition CS-only trials were begun initiating experimental extinction.

Periodic blood samples were drawn from the arterial catheter prior to and during the experiment for blood pH and gas analysis. Normal levels were maintained by controlled respiration.

Operant Conditioning Procedure. The Sandbox I logic panel was programmed to compare a reference voltage to the voltage emitted by mean coronary blood flow. When the two

voltages are equal, an event can be programmed to occur (in this case, the termination of stimuli). The reference voltage was visualized on the Visicorder along with mean coronary flow and the other cardiovascular measures. The reference voltage was manipulable by a hand control dial which, when turned clockwise, increased the required voltage change emitted by changes in coronary flow in order to match the reference and terminate the stimulus or stimuli.

The escape-avoidance paradigm was employed to shape decreases in coronary blood flow. Five animals were subjected to the training procedure and data are presented on four of these subjects. One of the five did not respond to any aspect of the procedure and was therefore eliminated from the analysis. It was suspected that respiratory-induced biochemical changes may have interfered with the cardiovascular responsivity of the animal.

The four animals who were successfully shaped to emit regular decreases in coronary blood flow were subjected to 75, 55, 100, and 45 acquisition trials respectively by the order in which they were run.

RESULTS

RESPONDENT CONDITIONING

The following time segments were analyzed as the critical temporal features of respondent habituation (HAB), acquisition (ACQ), and extinction (EXT): Baseline, Early CS, Late CS, UCS, and Post-CS (+UCS). Their temporal

definition, the response components to which they refer, and the symbols used to illustrate the results in subsequent figures are described in Table 2. These time segments were analyzed across trials for each of the three respondent conditioning procedures (habituation, acquisition, extinction) thus generating two-factor analyses of variance (ANOVA) with repeated measures on each factor for each of the six dependent measures. Habituation required 5 X 5 ANOVA's while acquisition and extinction each required 5 X 10 ANOVA's. Results of these analyses are subsequently described for each of the six dependent variables for which method of measurement, data form, and respective N's are indicated in Table 3.

Coronary Flow. Figure 1 illustrates the coronary response for each of five segments across respondent habituation and acquisition trials. Analyses of time segments, trials, and interaction effects during habituation are presented in Table 4. None of the F-ratios approach significance confirming the absence of any systematic response to the novelty of the CS as reflected in Figure 1. In acquisition, however, a dramatic increase in coronary flow to the UCS and rapidly to the CS is evident from an inspection of Figure 1. These conditioned and unconditioned increases across all time segments were confirmed by significant F-ratios for time segments and time segments X trials interaction (Table 5). The significant interaction most

likely reflects the profound change in the form of the recovery from UCS to post-stimulus intervals. The effect of trials is not revealed to be significant by this analysis because of the rapidity with which the CR emerges without further changes in magnitude. Inspection of Figure 1 reveals a trend toward a dissipation of the orienting CR which is replaced by an increased anticipatory CR in later acquisition. The total CR component of the time segment effect was found to be significant as reflected in Table 6. The trials effect is again washed out by the rapidity of conditioning and the significant interaction effect is lost by an exclusion of the u to p inverted-V recovery pattern.

When the UCS is withdrawn in extinction the significant time segment effect is lost for the b-e-l period (See Table 7) but remains when all time segments are included in the analysis (See Table 8). This suggests that the anticipatory CR is less resistant to extinction than the substitutive CR. Figure 2 illustrates these changes in the coronary flow response during extinction. However, there is a great deal of between-subject variation during extinction as reflected in mean squares values in Table 9. Much of this variation can be accounted for by one animal in particular who also contributes significantly to the deviation of Trial 6 in extinction (See Figure 2). There was no basis on which this subject could have been excluded from the analysis.

In summary, the respondent CR for coronary blood flow is a dramatic increase which develops quite early in acquisition. The CR is characteristically anticipatory in nature in that it consistently develops in close approximation to the onset of the UCS. While there are single-subject exceptions, the coronary CR is not particularly resistant to extinction from the perspective of grouped data.

Aortic Flow. Figure 3 illustrates the aortic flow response to habituation and acquisition. For habituation, neither the time segment nor the trials effect approaches statistical significance but their interaction is barely significant suggesting that the bi-phasic decrease-to-increase across trials is reliable (See Table 9). This analysis and inspection of Figure 3 reveal no systematic variation which might be interpreted as an unaltered orienting response.

A dramatic increase in aortic flow to the UCS and rapidly to the CS is clearly reflected in Figure 3 which is confirmed by a significant time segment F-ratio for the baseline through recovery (See Table 10) and for the baseline to late-CS segment (See Table 11). Once again, the significant time segment change in the absence of a corresponding trials effect seems to be a product of rapid learning (in this case, two-trial learning).

Figure 4 illustrates aortic flow response to the removal of the UCS across ten trials. As with coronary flow,

the anticipatory CR is sufficiently variant across extinction trials to eliminate the time segment effect for the baseline to late-CS period (See Table 12). However, the complete time segment analysis reveals a substitutive CR which appears to be more resistant to extinction (See Table 13).

To summarize, the conditioned aortic blood flow response is a consistent increase during both segments of the CS which appears to be moderately resistant to extinction.

Mean Blood Pressure. The blood pressure response to habituation and acquisition is illustrated in Figure 5. The lack of systematic variation across habituation trials is clearly reflected here and is confirmed by an absence of a significant F-ratio for any of the three sources of effects (See Table 14). The mean blood pressure increases to the UCS and CS is highly significant as reflected by the F-ratio for the complete time segment effect in Table 15. The significant interaction of time segment X trials reflects the bi-phasic increase to decrease mean of the total time segment across trials during acquisition. The baseline to late-CS (b-e-l) component of the total time segment is significant across trials as is the interaction effect again reflecting the bi-phasicity of the overall time segment mean (See Table 16). It appears from an examination of Figure 5 that both the orienting CR and the anticipatory CR share equally in their contribution to the

total CR configuration.

Additionally, both CR components extinguish as rapidly as they emerged and this is clearly reflected in Figure 6. F-ratios confirm the rapid dissipation of the CRs for both the total time segment effect and the baseline to late-CS segment (See Table 17 and 18). Furthermore, the substitutive CR is never clearly established in early extinction as with other cardiovascular responses in the present experiment.

In summary, for blood pressure the respondent CR is a dramatic increase during early and late periods of the CS segment. The response is acquired quite rapidly and manifests virtually no resistance to extinction.

Heart Rate. Figure 7 illustrates the HR response to habituation and acquisition. Inspection of this graph indicates what would appear to be an initial orienting response of cardioacceleration whose magnitude decreases over the five habituation trials. However, systematic variation during habituation only approaches statistical confirmation as indicated in Table 19 which examines the total time segment variation.

Further examination of Figure 7 reveals the emergence of a dramatic acceleratory orienting CR and decelerating anticipatory CR which is possibly more a compensatory than a true anticipatory response. Analysis of variance indicates a significant total time segment effect with a

significant time segment X trials interaction (See Table 20). The development of the orienting CR is highlighted in Table 21 in which the time segment acceleration is even more dramatic and a significant trials effect suggests that the cardioacceleration increases in magnitude over time. The time segment X trials interaction is also barely significant. Table 22 presents F-ratios for the "compensatory" deceleration in the e-1 time segment. The magnitude of deceleration is not significant but the combined mean across trials is significant as well as the time segment X trials interaction.

Heart rate extinction trials are illustrated in Figure 8. The orienting CR is dramatically resistant to extinction as reflected in the highly significant time segment F-ratio in Table 23. Additionally, the "compensatory" decelerative component of the early to late-CS (e-1) segment has become much more uniform. The significant magnitude of this deceleration is confirmed by the time segment F-ratio of Table 24. The combined mean for the e-1 time segment however is decreasing significantly across trials as reflected also in Table 24 (Trials F-ratio). Analysis of the total time segment effect further confirms this highly consistent and statistically reliable configuration whose overall mean decreases significantly across trials (See Table 25).

To summarize, the aversive respondent CR for heart rate is an "orienting" acceleration and a late segment deceleration of possible compensatory origins. The acceleratory component is extremely resistant to extinction whereas the decelerative component is significantly less consistent in extinction.

Stroke Volume. Figure 9 illustrates the stroke volume response to habituation and acquisition. No systematic variation in stroke volume to the novelty of the CS can be detected during habituation and this is confirmed by the F-ratios of Table 26. In acquisition, however, a significant time segment effect emerges in the absence of a trials or time segment X trials interaction. This is not only significant for the total time segment analysis (Table 27) but also for the V-shaped baseline to late-CS (b-e-l) period (Table 28). The orienting CR portion of this V-configuration is undoubtedly a product of the pronounced cardioacceleratory orienting CR.

Figure 10 illustrates the change of these configurations during extinction. The significant early CR is lost in extinction as reflected in the F-ratios of Table 29 but the total time segment configuration remains barely significant as indicated by the analysis described in Table 30.

Peripheral Resistance. The peripheral resistance response to habituation and acquisition is illustrated in Figure 11. There are no statistically significant trends

for the complete time segment response in either habituation or acquisition (See Tables 31 and 32). However, inspection of Figure 11 reveals the emergence of a consistent V-shaped configuration in later acquisition (See trials 6-10). The small N and large between-subject variation in this response may account for the lack of a significant F-ratio for the CR component of this response also (See Table 33). However, the orienting CR and anticipatory CR pattern remain for most of extinction (See Figure 12) and this baseline to late-CS (b-e-1) time segment change across extinction trials is statistically reliable as indicated in Table 34. The conditioned peripheral resistance response is therefore shown to be quite resistant to extinction.

Correlational Analyses

Direct Measures. Correlation coefficients were computed to determine the relationship of coronary flow to each of the five direct and derived cardiovascular measures for each trial of habituation, acquisition, and extinction using the 30-sec stimulus period as the target interval. Ten 3-sec segments of the stimulus period (using five animals for whom data on all six variables were complete) were employed for the correlational analysis. The resulting number of observations per correlation coefficient was 50.

Figure 13 presents the coefficients of correlation for coronary flow with each of the other direct cardiovascular measures: blood pressure, aortic flow, and heart

rate. As can be seen, the correlation of coronary flow with mean blood pressure is highly significant across all trials of habituation, acquisition, and extinction. Coronary flow and aortic flow appear marginally correlated in habituation but "uncouple" dramatically during acquisition. Coronary flow and heart rate do not correlate in any significant systematic fashion.

The coefficients of correlation for coronary flow with the two derived cardiovascular measures are presented in Figure 14. The correlation of coronary flow with peripheral resistance is not particularly high during habituation but increases to statistically significant levels during acquisition and returns to less than significant levels during extinction. The multi-trial configuration for peripheral resistance more closely resembles its mean blood pressure counterpart than aortic flow. Stroke volume correlation with coronary flow, on the other hand, is more similar to the aortic flow curve than to heart rate from which it is derived. In general, stroke volume does not correlate well with coronary flow.

Table 35 summarizes the results of aversive respondent conditioning on six cardiovascular measures.

OPERANT CONDITIONING

Four ss were successfully trained to decrease coronary blood flow in order to escape from and avoid shock. Data were tabulated for analysis by measuring a four second

pre-stimulus baseline average which was compared to the value of each variable at the point on which the tone and shock or tone were terminated (delivery of negative reinforcement). With heart rate, the baseline value was compared to the four-second period defined by two seconds to each side of reinforcement delivery. The difference between values at baseline and values at reinforcement will hereafter be referred as "period" effects. Thus the effect of period is equivalent to the amount of change in each variable which was reinforced on any given trial. For both individual and group analyses and illustrations, trials of operant acquisition were Vincentized into fifths of conditioning. The resultant group design investigated the effects of two independent variables, period and Vincentized trials, on each of three available dependent measures: coronary blood flow, central aortic blood pressure, and heart rate. The results were analyzed by two-factor analyses of variance (2X5) with repeated measures on both factors. Data for each cell were generated by reducing each S's baseline and reinforced values to mean values for each of the five Vincentized segments of acquisition. The diagrams of Table 36 and 37 illustrate precisely how the data were reduced and arranged for the analyses of variance on each of the three dependent variables.

Individual Results. Figure 15 illustrates the acquisition of decreases in coronary blood flow across fifths of

trials for a typical subject. Corresponding changes in aortic blood flow, blood pressure, and heart rate are also presented. Decreases in coronary blood flow of 10-15% are rapidly shaped within 15 trials and maintained over the additional 60 trials for this subject. In early conditioning the decreases in coronary flow are accompanied by a decrease in blood pressure, an increase in aortic flow, and one to two extrasystoles. As conditioning proceeds, however, the influences of blood pressure and aortic flow dissipate while increases in heart rate continue to accompany the coronary decreases.

Although the magnitude of the coronary decreases can not be shaped further beyond the first fifth of conditioning, the ease with which the response is emitted improves with practice. Latencies of the shaped response were transformed to response speed by the formula, $\frac{1}{\text{latency}} \times 1000$, and a one-way analysis of variance was performed on the five segments of conditioning. The results of the analysis indicated that the improvement in performance was statistically reliable [$F(4,56) = 32.17$, $P < .005$]. A correlated indication of improvement across trials is that only four shocks were avoided during the first 15 trials, while 11 of 15 were avoided during the last segment of conditioning.

In one subject, coronary decreases of large magnitude were shaped within 100 trials of acquisition. The mean decreases and the corresponding changes in heart rate and

blood pressure are illustrated in Figure 16. In this animal, decreases in blood pressure continue to accompany the coronary decrease into late conditioning. Heart rate acceleration is also evident during the final segment of acquisition. A sample trial of late acquisition is presented in Figure 17. On this trial one of the largest magnitude responses was emitted. The accompanying changes in heart rate and blood pressure can be easily detected from an inspection of this Figure.

Group Results. Grouped data for the four animals who were successfully shaped to emit decreases in coronary flow are presented in Figure 18. The average magnitude of the shaped decreases is 15-20%. The corresponding percentages of change in heart rate and blood pressure are also presented in this Figure.

Figure 19 illustrates the means of coronary flow for baseline to reinforcement across fifths of conditioning. A 2 X 5 analysis of variance with repeated measures was performed on these data and the results are presented in Table 38. The magnitude of the decreases from baseline to reinforcement is statistically significant ($P \leq .05$) while the trials and trials X period interaction do not approach significance.

Figure 20 illustrates the corresponding changes in heart rate from baseline to reinforcement periods. An increase is evident in all of the five segments of conditioning

whose magnitude is statistically significant ($P \leq .05$). An increase in heart rate across segments of acquisition is reflected in Figure 20 but not statistically confirmed (See Table 39). However, the interaction between period and trials is significant ($P \leq .05$) indicating that one of these changes is dependent upon the other. The magnitude of changes in periods is dependent upon the segment of training. This interaction is also influenced by the progressively increasing basal values of heart rate across the five segments of conditioning as reflected in Figure 20.

Figure 21 presents corresponding changes in blood pressure from baseline to reinforcement. It is clear from this illustration that changes in blood pressure influence the coronary operant particularly in earlier acquisition. The decrease in blood pressure is virtually lost by the final segment of conditioning thus eliminating the effect of period (See Table 40). Also, there is no significant change across trials. However, the gradual dissipation of decreases in blood pressure from baseline to reinforcement across trials is confirmed by the significant F -ratio for the interaction of period and trials (Table 40).

Figure 22 illustrates the grouped latency and avoidance results. A one-way analysis of variance was calculated on transformed latency data and indicated that the increasing speed with which the responses achieved reinforcement was highly reliable [$F(4,216)=65.71$, $P \leq .001$]. As

latencies improve, so does the frequency with which subjects were able to avoid the onset of shocks. This is clearly highlighted in Figure 22.

DISCUSSION

RESPONDENT CONDITIONING

The results of the present experiment confirm many of the findings of earlier studies investigating the cardiovascular response to the aversive respondent conditioning paradigm. Additionally the present results provide new information about some of the less frequently studied response components.

The results indicating a dramatic respondent unconditioned increase in coronary blood flow and rapidly developed conditioned increases confirm the preliminary findings of Bergamaschi, et.al., (1973a, 1973b) who report that coronary flow increases to stressful events and stimuli associated with stress. Corresponding conditioned increases in cardiac output (aortic flow) and heart rate with a decrease in peripheral resistance are also confirmed in the present investigation. However, their report of no significant change in aortic pressure stands in marked contradistinction to the dramatic changes found here for mean blood pressure which was also central aortic in origin.

Of particular relevance to an understanding of the coronary response in the present investigation are the correlations with other cardiovascular events. The

"uncoupling" of coronary flow from aortic flow in acquisition is a fascinating phenomenon which suggests that the coronary system is capable of operating quite independently of cardiac output under circumstances of increased demands. This may well mean that the coronary arteries can increase the draw on blood available at the aorta irrespective of whether or not the available supply increases correspondingly. However, this relative independence does not appear to extend to perfusion pressure as reflected by the mean central aortic blood pressure correlations with coronary flow. Correlations between these two measures decrease during acquisition, and perhaps, if acquisition were extended a similar uncoupling of coronary flow and blood pressure might also develop.

Interestingly the correlations of coronary flow with blood pressure remain highly significant irrespective of the procedural interval. However, correlations with peripheral resistance appear to depend upon the type of procedural interval. More specifically, nonsignificant correlations during habituation change to highly significant ones during acquisition and then return to less than significant values during extinction. This is in fascinating contrast to the coronary flow-aortic flow correlations whose dynamics are clearly opposite. The relatively high correlations of habituation are lost at approximately identical times that the peripheral resistance correlations

emerge. Also in contrast to the correlations with blood pressure, those with peripheral resistance drop appreciably during the latter half of acquisition again raising the question of what might happen if acquisition were extended by several trials. This may mean that the correlations of peripheral resistance change first under learning conditions paralleling the uncoupling of aortic flow (which is an integral component of the PR computation). Further study of these phenomena with extended acquisition may generate hierarchies of responses whose rank is determined by their relative "resistance to uncoupling". In summary, the major finding of the respondent conditioning investigation is that coronary blood flow increases dramatically during stress and the anticipation of stress. An interpretation of operant conditioning in which stress reduction is used to reinforce changes in coronary flow depends to an important extent on an awareness of this result. Specifically, attempts to operantly condition increases in coronary blood flow will be confounded by respondently-elicited increases when the presentation and termination of stressful stimuli are employed as reinforcers. Conversely, attempts to operantly condition decreases in coronary blood flow will be resultingly more difficult for the same reason. So too would the achievement of operant decreases be all the more profound.

Other Cardiovascular Conditioning. The highly consistent and statistically reliable conditioned increases in HR replicate the findings of a preponderance of studies which have firmly established cardioacceleration as the aversive CR for dogs (e.g., Fitzgerald, 1966; Obrist, et. al., 1972). The length of the CS in the present study was unlike most previous research and accounts for the probable compensatory cardiodeceleration of the late-CS segment. Interestingly, stroke volume changes are intimately tied to this bi-phasic HR CR. The tachycardia of the early-CS segment closely corresponds to the decreased stroke volume which is known to be a product of the reduced pumping efficiency of the increased rate. (This increased work undoubtedly has a systematic contribution to the late coronary flow CR but its exact nature cannot be adequately determined without a careful experimental manipulation of the events in question). As the HR rebounds from the tachycardia by late-CS, so returns the pumping efficiency reflected by increased stroke volume.

Further replication is also provided for previous studies investigating the vascular response to the aversive conditioning paradigm who have rather uniformly found conditioned blood pressure increases for dogs and most other species (e.g., Newton, 1967). Of particular interest for the BP response in the present study is the incredibly weak resistance to extinction of the response. One-trial

learning is paralleled by practically one-trial extinction! Most studies have not included habituation and extinction data for this measure. The present experiment was the first to examine these additional procedures.

Finally, the peripheral resistance response provides an interesting additional cardiovascular measure of aversive conditioning despite the absence of strong statistical reliability. A cursory analysis of the PR response might appear contradictory to the findings for BP. That is, how can highly significant conditioned increases in BP parallel conditioned decreases in resistance? The propable answer is that the increase in cardiac output more than compensates for the increased pressure and it is the cardiac output (aortic-flow) which contributes most significantly to the PR computation. Dynamically then, increased aortic flow essentially forces perfusion against an increased pressure gradient the net effect of which is a decrease in peripheral resistance.

OPERANT CONDITIONING

The results of the operant study indicate that decreases in coronary blood flow can be shaped by using stimuli which have been demonstrated to increase respondent blood flow. As such, the present investigation is the only study of its kind in which coronary blood flow was manipulated by operant conditioning. It is one of four studies of operant conditioning involving blood flow in an

infrac human species and the present results clearly replicate the findings of the other three studies. DiCara & Miller (1968c) achieved very small relative changes in blood flow to the ears and Miller & DiCara (1968b) inferred operant control of renal blood flow by manipulating urine formation in the kidney. In neither of these studies were additional measures of other cardiovascular functions included. In the present investigation the mediating influence of heart rate and blood pressure were systematically examined.

Carmona, Miller, & Demierre (1974) demonstrated operant control of gastric perfusion in an investigation quite similar to the present one. The escape-avoidance paradigm was also employed and small but consistent increases and decreases in gastric blood flow were achieved by reinforcing changes measured by the density of light passing through the stomach wall. A footnote to their study indicated an inability to replicate these and other findings relative to blood flow particularly. The present results provide replication of their findings under circumstances in which blood flow was measured more directly (flow probe).

As indicated earlier, operant control of heart rate has been replicated a number of times in several different laboratories using both appetitive and aversive control procedures. At present, replications are lacking for

operant conditioning of blood pressure. DiCara & Miller (1968b) demonstrated bi-directional control of blood pressure which was replicated by Pappas, DiCara, & Miller (1970) using both unrestrained and then curarized preparations. Since then however, studies of blood pressure have only been able to demonstrate control in the confounded direction complicated by the respondent artifact of aversive procedures (Plumlee, 1969; Harris, Findley, & Brady, 1971). In three of four animals of the present study it was difficult to determine how much of the achieved change in coronary flow could be accounted for by the mediation of extrasystoles and slight decreases in central aortic blood pressure. The decreased aortic pressure can mediate part of the response by reducing the coronary perfusion pressure while increases in heart rate can have a similar effect by reducing the diastolic time during which filling of the left coronary artery occurs. It is impossible to determine what proportion of the response for these animals was resultingly passive and what proportion constituted active coronary vasoconstriction. On the other hand, the results with the fourth subject whose performance is depicted in Figures 16 and 17 can only be interpreted as active vasoconstriction. Decreases of such large magnitude could not have been passively mediated by the relatively slight changes in heart rate and blood pressure shown in Figures 16 and 17. Collectively, these data are submitted as evidence that

coronary blood flow can be manipulated by stressful operant contingencies. Additionally, performance of the coronary operant can improve with practice as evidenced by the increasing speed with which the response is emitted over trials and the increasing frequency of avoidance responses across segments of conditioning.

The specific negative reinforcement employed in the present study is only one of several types of operant consequences which might be used to control behavior. As an aversive conditioning procedure, its effectiveness in controlling coronary blood flow would suggest that the response might also be manipulable by other aversive consequences. Furthermore, the results also suggest that the response could be controlled by appetitive reinforcers if indeed learning, as a general phenomenon, has been demonstrated in the present study.

IMPLICATIONS OF THE RESULTS

The results of the present investigation have profound implications of interest to more than one scientific discipline.

Conditioning and learning have been topics of particular concern to experimental psychologists. One issue which has received a great deal of attention in the literature since Miller's (1969) pioneering effort is the question regarding the nature of learning, and more specifically, whether or not operant is characteristically distinct from

respondent learning. Traditionally, the two have been regarded as involving different processes primarily because of the distinctions reflected in Table 41. In demonstrating that an autonomically-mediated visceral behavior like coronary blood flow can be controlled operantly (read, "voluntarily"), several of these distinctions are resultingly blurred so that the question regarding "process" is reduced to a question of "procedure". That is, perhaps the only meaningful distinction between respondent and operant learning is simply in the nature of the procedure which are used to achieve the change in behavior.

Miller's (1969) work was pioneering in that it initiated re-conceptualizing these distinctions. However, his findings and their implications are currently undergoing considerable scrutiny because of indications that Miller and his students more recently have been unable to replicate their results (see, for example, Miller & Dworkin, 1974 and Carmona, Demierre, & Miller, 1974). In this important respect, the present study is the only documented replication of their findings regarding operant control of vasomotor function in the curarized infrahuman laboratory subject.

Many of the theoretical issues of experimental psychology overlap significantly with those of physiological psychology. Additionally, however, the physiological psychologist is concerned with the mechanics of neurological

regulation particularly in connection with the neurological mediation of learning. As with distinctions between types of learning, similar convictions have been traditionally held regarding the functional differentiation between the autonomic and central nervous system as well as their interaction. While the results of the present study do not specifically provide new information on this issue, they suggest that the two systems can operate similarly and that the autonomic nervous system may well be capable of mediating highly specific visceral activity which can be independent of otherwise related somatic events. In any event, the paradigm employed in the present investigation provides a methodologically sound vehicle through which nervous regulation can be productively examined. Additionally the coronary vascular response seems likely to be a productive dependent measure because of its well-documented richness of autonomic innervation and because the present results strongly suggest a remarkable degree of sensitivity of the coronary system.

A major finding of the present study is that the coronary system can be so responsive to environmental events, particularly those of a stressful nature. This corroborates and extends the early work in Gregg's laboratory (Rayford, Kauri, & Gregg, 1965) which unfortunately has received very little systematic follow-up. An exception is the investigation of Bergamaschi, Caravaggi, Mandelli, &

Shanks (1973) who crudely examined the coronary response to aversive events. As indicated above, their results were largely replicated in the present investigation. In any event, it is curious indeed that so little research is conducted in which the effects of stress on coronary circulation are examined. This is particularly surprising in light of the fact that there is nearly universal agreement amongst physicians and cardiologists that stress can play a major role in the etiology and exacerbation of coronary heart disease and myocardial infarction.

The findings of the present investigation regarding operant decreases in coronary blood flow could be quite important to an understanding of the etiology of coronary pathophysiology. As indicated in the Introduction, angina pectoris and myocardial infarction are problems of coronary blood flow. The Prinzmetal syndrome is one type of angina which can be found in patients without significant atherosclerotic disease. Moreover there are incidences of myocardial infarction in the absence of such disease as well. It is conceivable that the present results provide one possible mechanism which can account for these otherwise inexplicable clinical events. Perhaps the blood flow problem in those situations is one of learned vasoconstriction which is shaped and increased in magnitude with the continued practice which is possible in the natural environment. One likely reinforcer could be anxiety-reduction

which not only parallels the type of reinforcement used in the present investigation but which is known to shape neuroses such as phobias, obsessions, and compulsions. Anxiety reduction as a reinforcer is an extremely powerful consequence producing significant resistance to extinction.

Most important from the perspective of the author's specialization is the implication of this work to clinical psychology. This discipline has evolved from largely a speculative endeavor to the present-day more empirically oriented approach typified by behavior therapy which is based on the kinds of conditioning principles investigated in the present study. A growing interest in the clinical application of operant principles combined with Miller's (1969) ingenious application of operant techniques to the presumed involuntary behaviors of the viscera provided the stimulus and the substantive basis for the development of biofeedback therapies (Engel, 1972; Shapiro, et.al., 1970; Sargent, et.al., 1974). These developments paralleled, and to some extent, stimulated the development of interest in self-regulation by clinical psychologists. The findings of the present investigation suggest that techniques of biofeedback and self-regulation might well be applied to a problem of blood flow which has more serious adverse health consequences than all other diseases combined.

Table 1
Descriptive Summary of Animal Studies on Operant
Conditioning of Cardiovascular Function

<u>Species</u>	<u>N</u>	<u>Paradigm</u>	<u>Reinforcer</u>	<u>Immobilization</u>	<u>Findings</u>	<u>Authors</u>
Rats	19▲ 17▼	Reward shaping (no S ^D)	ESB	Curare	▲&▼ HR, $\bar{X}$ = 5%▲	Trowill (1967)
Rats	12▲ 12▼	Reward shaping (S ^D)	ESB	Curare	▲&▼ HR, $\bar{X}$ = 20%▲ with extended training	Miller & DiCara (1967)
Rats	6▲ 6▼	Escape- avoidance	CS and/or shock term- ination	Curare	▲&▼ HR, $\bar{X}$ = 20%▲	DiCara & Miller (1968a)
Rats	6▲ 6▼	Escape- avoidance	CS and/or shock term- ination	Curare	12%▲▲ HR 23%▲▼ HR 3 mos. retention	Miller & DiCara (1968a)
Rats	8▲ 8▼	Escape- avoidance	CS and/or shock term- ination	Curare and free move- ment	5%▲▲, 16%▲▼ HR (curarized) to 11%▲▲, 22%▲▼ HR (free movement)	DiCara & Miller (1969)
Rats	7▲ 7▼	Escape- avoidance	CS and/or shock termination	Curare and free move- ment	0%▲▲, 16%▲▼ HR (free movement) to 6%▲▲, 13%▲▼ HR (curarized)	Miller & DiCara (1969)

Table 1 (Cont'd.)

<u>Species</u>	<u>N</u>	<u>Paradigm</u>	<u>Reinforcer</u>	<u>Immobilization</u>	<u>Findings</u>	<u>Authors</u>
Rats	7▲ 7▼	Escape-avoidance	CS and/or shock termination	Curare and free movement	9%▲▲, 8%▲▼ HR (curarized) 4%▲▲, 9%▲▼ HR (free movement)	DiCara & Weiss (1969)
Rats	6▲ 6▼	Reward shaping (SD)	ESB	Curare	Small but highly consistent HR ▲&▼ 4 sessions of adaptation, acquisition, & extinction	Hothersall & Brener (1969)
Rats	10▲ 10▼	Reward shaping (SD)	ESB	Curare	14%▲▲, 9%▲▼ HR Pre-training in SD bar-press for ESB did not affect HR conditioning	Slaughter, Hahn, & Rinaldi (1970)
Rats	22▲ 22▼	Reward shaping (compound SD)	ESB	Curare	9%▲▲, 8%▲▼ HR ▲Ss showed ▲ in endogenous brain & cardiac catecholamines	DiCara & Stone (1970)
Rats	12▲ 12▼	Escape-avoidance	CS and/or shock termination	Curare	HR▼ primarily; decorticates did not manifest HR conditioning; poor performance by normals	DiCara, Braun, & Pappas (1970)

Table 1 (Cont'd)

<u>Species</u>	<u>N</u>	<u>Paradigm</u>	<u>Reinforcer</u>	<u>Immobilization</u>	<u>Findings</u>	<u>Authors</u>
Rats	46	Punishment or reward	Shock or ESB	Curare	▲&▼ of P-R and P-P intervals of cardiac cycle independent of R-R	Fields (1970)
Rats	20▲ 20▼	Avoidance	Aversive CS termination	Curare and free movement	▲&▼ HR; Ss pre-trained to be im-mobile had greater during curare HR training	Goesling & Brener (1972)
Rats	19	Punishment (unsignalled)	Shock	Curare	▼HR w/resistance to extinction; ▲HR difficult, successful in 3/10; other 7 actually▼	Roberts, et. al. (1974)
Rats	10▲ 11▼	Reward shaping	Infrared heat in cold chamber	Curare	▲&▼ HR empirically corrected for changes in body temperature	Cabanac & Serres (1976)
Dogs	?	Escape-avoidance	CS and/or shock termination	Curare	▲&▼ HR; ▼more difficult to achieve	Black (1968)
Monkeys	1▲-▼ 2▼-▲	Within-S bi-direct. punishment	Shock	Restraint	▲-▼ & ▼-▲ HR; large magnitude w/o corresponding changes in blood pressure	Engel & Gottlieb (1970)

Table 1 (Cont'd)

<u>Species</u>	<u>N</u>	<u>Paradigm</u>	<u>Reinforcer</u>	<u>Immobilization</u>	<u>Findings</u>	<u>Authors</u>
Monkeys	4	Avoidance	Aversive CS termination	Restraint	▲&▼ HR; BP r+ with ▲&▼; r+'s ▲ w/training for HR▼ but not for HRA	Engel (1974)
Monkeys	4	Avoidance	Aversive CS termination	Restraint	▲&▼ HR w/ $\Delta\bar{X}$ =15 bpm Operantly reversed responsdently conditioned HR w/o affecting responsdently conditioned BP response	Ainslie & Engel (1975)
Rats	7▲ 7▼	Escape-avoidance	CS and/or shock termination	Curare	22.3%▲▲SBP 19.2%▲▼SBP Low correlations between BP & HR	DiCara & Miller (1968b)
Rats	9▲ 8▼	Escape-avoidance	CS and/or shock termination	Free movement to curare	28.4 mm/Hg ▲ & 15.1 mm/Hg ▼ maxium w/free move. 10.3 mm/Hg ▲ & 10.9 mm/Hg $\bar{X}$ ▼'s during later curare	Pappas, DiCara, & Miller (1970)
Monkeys	4 (all ▲)	Avoidance	Aversive CS	Restraint	Up to 60 mm/Hg▲	Plumlee (1969)

Table 1 (Cont'd)

<u>Species</u>	<u>N</u>	<u>Paradigm</u>	<u>Reinforcer</u>	<u>Immobilization</u>	<u>Findings</u>	<u>Authors</u>
Baboons	2 Δ	Shock avoidance & food reward	CS termination & food	Restraint	50-60 mm/Hg Δ DBP with corresponding changes in SBP	Harris, Findley, & Brady (1971)
Rats	6 Δ 6 ∇	Reward shaping	ESB	Curare	Δ & ∇ in relative vasodilation in right vs left ear, and vice versa	DiCara & Miller (1968c)
Rats	4 Δ 4 ∇	Reward shaping	ESB	Curare	Δ & ∇ in renal urine formation w/corresponding Δ & ∇ in renal blood flow	Miller & DiCara (1968b)
Rats	5 Δ 5 ∇	Escape-avoidance	CS and/or shock termination	Curare	Extremely small but consistent Δ & ∇ in gastric perfusion (blood flow)	Carmona, Miller, & DeMierre (1974)

Δ = (delta) change(s)

Δ = increase(s)

∇ = decrease(s)

HR=heart rate

SBP = systolic blood pressure

DBP = diastolic blood pressure

ESB = electrical stimulation of the brain

r+ = positive correlation

TABLE 2

TIME SEGMENTS WITHIN TRIALS OF RESPONDENT HABITUATION, ACQUISITION, AND EXTINCTION

<u>SEGMENT</u>	<u>DEFINITION</u>	<u>FIGURES SYMBOLS</u>	<u>RESPONSE COMPONENT</u>
Baseline	9-sec. period preceding CS onset	b, ○	baseline
Early CS	First 9-sec. period of CS interval	e, ●	Orienting R (HAB) Orienting CR (ACQ & EXT)
Late CS	Second 9-sec. period of CS Interval	l, ●	Orienting R (HAB) Anticipatory CR (ACQ & EXT)
UCS	9-sec. period of the UCS interval	u, ▲ (ACQ) ● (HAB, EXT)	Orienting R (HAB) UCR (ACQ) Substitutive CR (EXT)
Post-CS (& UCS)	9-sec. period following offset of CS (& UCS)	p, ○	Recovery

TABLE 3

DESCRIPTION OF DEPENDENT VARIABLES

<u>DIRECT MEASURES</u>			
<u>Dependent Variables</u>	<u>Method</u>	<u>Form</u>	<u>N</u>
Coronary Flow (CF)	Electromagnetic Flow Probe	cc's/min	8
Aortic Flow (AF)	Electromagnetic Flow Probe	liters/min	5
Mean Blood Pressure (MBP)	Catheterized Transducer	mm/Hg	10
Heart Rate (HR)	Contralateral Electrodes	bpm	10
<u>DERIVED MEASURES</u>			
<u>Dependent Variables</u>	<u>Method</u>	<u>Form</u>	<u>N</u>
Stroke Volume (SV)	$\frac{AF}{HR}$	cc's/stroke	5
Peripheral Resistance (PR)	$\frac{MBP}{AF}$	dynes-sec/cm ⁵	4

TABLE 4

ANALYSIS OF VARIANCE: CF-HAB (All Segments)

Source	df	MS	F
Time Segments (A)	4	591.60	0.26
Trials (B)	4	4036.61	1.62
Subjects (C)	7	1200.24	
A X B	16	1342.92	1.18
A X C	28	2281.43	
B X C	28	2485.78	
A X B X C	112	1138.77	

TABLE 5

ANALYSIS OF VARIANCE: CF-ACQ (All Segments)

Source	df	MS	F
Time Segments (A)	4	75328.62	5.47*
Trials (B)	9	4806.26	0.97
Subjects (C)	7	1072617.00	
A X B	36	3292.55	2.73**
A X C	28	13762.55	
B X C	63	4951.06	
A X B X C	252	1205.41	

* P $\leq$.005** P $\leq$.001

TABLE 6

ANALYSIS OF VARIANCE: CF-ACQ (b, e, l Components)

Source	df	MS	F
Time Segments (A)	2	27150.92	4.97*
Trials (B)	9	4473.42	0.99
Subjects (C)	7	460407.40	
A X B	18	834.88	1.31
A X C	14	5467.58	
B X C	63	4539.32	
A X B X C	126	638.41	

* $P < .025$

TABLE 7

ANALYSIS OF VARIANCE: CF-EXT (b, e, l Components)

Source	df	MS	F
Time Segments (A)	2	9897.19	3.63
Trials (B)	9	6948.07	1.75
Subjects (C)	7	786165.60	
A X B	18	535.70	1.26
A X C	14	2727.90	
B X C	63	3970.61	
A X B X C	126	426.61	

TABLE 8

ANALYSIS OF VARIANCE: CF-EXT (All Segments)

Source	df	MS	F
Time Segments (A)	4	13689.83	5.06*
Trials (B)	9	13273.60	1.24
Subjects (C)	7	1424799.00	
A X B	36	823.80	1.34
A X C	28	2706.02	
B X C	63	10697.15	
A X B X C	252	613.64	

* $P < .005$

TABLE 9

ANALYSIS OF VARIANCE: AF-HAB (All Segments)

Source	df	MS	F
Time Segments (A)	4	0.26	1.73
Trials (B)	4	0.60	0.76
Subjects (C)	4	57.78	
A X B	16	0.65	1.99*
A X C	16	0.15	
B X C	16	0.79	
A X B X C	64	0.33	

* $P < .05$

TABLE 10

ANALYSIS OF VARIANCE: AF-ACQ (All Segments)

Source	df	MS	F
Time Segments (A)	4	1.55	9.29*
Trials (B)	9	0.16	0.97
Subjects (C)	4	169.29	
A X B	36	0.52	1.10
A X C	16	0.17	
B X C	36	0.17	
A X B X C	144	0.48	

* $P < .001$

TABLE 11

ANALYSIS OF VARIANCE: AF-ACQ (b, e, l Components)

Source	df	MS	F
Time Segments (A)	2	0.60	47.44*
Trials (B)	9	0.06	0.44
Subjects (C)	4	95.03	
A X B	18	0.04	1.83
A X C	8	0.01	
B X C	36	0.13	
A X B X C	72	0.02	

* $P < .001$

TABLE 12

ANALYSIS OF VARIANCE: AF-EXT (b, e, 1 Components)

Source	df	MS	F
Time Segments (A)	2	0.88	6.42
Trials (B)	9	0.25	0.87
Subjects (C)	4	77.44	
A X B	18	0.04	1.14
A X C	8	0.14	
B X C	36	0.29	
A X B X C	72	0.03	

TABLE 13

ANALYSIS OF VARIANCE: AF-EXT (All Segments)

Source	df	MS	F
Time Segments (A)	4	0.60	5.13*
Trials (B)	9	0.47	1.15
Subjects (C)	4	133.14	
A X B	36	0.47	0.94
A X C	16	0.12	
B X C	36	0.41	
A X B X C	144	0.50	

* $P < .01$

TABLE 14

ANALYSIS OF VARIANCE: BP-HAB (All Segments)

Source	df	MS	F
Time Segments (A)	4	25.92	0.36
Trials (B)	4	45.67	0.13
Subjects (C)	9	7437.78	
A X B	16	50.76	1.10
A X C	36	71.35	
B X C	36	350.65	
A X B X C	144	46.08	

TABLE 15

ANALYSIS OF VARIANCE: BP-ACQ (All Segments)

Source	df	MS	F
Time Segments (A)	4	10980.69	24.61*
Trials (B)	9	680.10	1.52
Subjects (C)	9	14595.48	
A X B	36	435.07	4.94*
A X C	36	446.24	
B X C	81	448.62	
A X B X C	324	88.00	

* $P < .001$

TABLE 16

ANALYSIS OF VARIANCE: BP-ACQ (b, e, l Components)

Source	df	MS	F
Time Segments (A)	2	4347.21	10.27*
Trials (B)	9	734.86	1.74
Subjects (C)	9	6864.67	
A X B	18	117.65	2.23
A X C	18	423.17	
B X C	81	422.09	
A X B X C	162	52.63	

* $P < .025$

TABLE 17

ANALYSIS OF VARIANCE: BP-EXT (All Segments)

Source	df	MS	F
Time Segments (A)	4	226.49	1.70
Trials (B)	9	217.79	0.89
Subjects (C)	9	11628.13	
A X B	36	42.23	1.15
A X C	36	133.54	
B X C	81	245.28	
A X B X C	324	36.85	

TABLE 18

ANALYSIS OF VARIANCE: BP-EXT (b to l Components)

Source	df	MS	F
Time Segments (A)	1	731.02	2.60
Trials (B)	9	65.71	0.60
Subjects (C)	9	4352.76	
A X B	9	75.25	1.17
A X C	9	280.96	
B X C	81	110.11	
A X B X C	81	64.44	

TABLE 19

ANALYSIS OF VARIANCE: HR-HAB (All Segments)

Source	df	MS	F
Time Segments (A)	4	503.67	2.61
Trials (B)	4	465.35	0.74
Subjects (C)	9	9376.94	
A X B	16	148.45	1.01
A X C	36	193.10	
B X C	36	628.07	
A X B X C	144	147.17	

TABLE 20

ANALYSIS OF VARIANCE: HR-ACQ (All Segments)

Source	df	MS	F
Time Segments (A)	4	4720.55	2.91*
Trials (B)	9	202.72	0.36
Subjects (C)	9	26108.62	
A X B	36	941.09	2.75**
A X C	36	1623.97	
B X C	81	559.09	
A X B X C	324	342.11	

* $P \leq .05$ ** $P \leq .001$

TABLE 21

ANALYSIS OF VARIANCE: HR-ACQ (b to e Components)

Source	df	MS	F
Time Segments (A)	1	6766.98	9.98*
Trials (B)	9	1033.75	3.16**
Subjects (C)	9	8278.97	
A X B	9	763.76	2.34***
A X C	9	678.31	
B X C	81	327.53	
A X B X C	81	326.06	

* $P < .01$ ** $P < .025$ *** $P < .05$

TABLE 22

ANALYSIS OF VARIANCE: HR-ACQ (e, 1 Components)

Source	df	MS	F
Time Segments (A)	1	1200.71	1.67
Trials (B)	9	1655.61	4.22*
Subjects (C)	9	11437.14	
A X B	9	719.58	2.17**
A X C	9	717.01	
B X C	81	392.04	
A X B X C	81	332.15	

* $P \angle .01$ ** $P \angle .05$

TABLE 23

ANALYSIS OF VARIANCE: HR-EXT (b to e Components)

Source	df	MS	F
Time Segments (A)	1	10999.74	31.17*
Trials (B)	9	460.86	1.85
Subjects (C)	9	11255.72	
A X B	9	127.55	0.86
A X C	9	352.88	
B X C	81	248.70	
A X B X C	81	148.81	

* $P \leq .001$

TABLE 24

ANALYSIS OF VARIANCE: HR-EXT (e, 1 Components)

Source	df	MS	F
Time Segments (A)	1	951.76	7.97*
Trials (B)	9	602.03	2.49*
Subjects (C)	9	12566.43	
A X B	9	161.28	0.96
A X C	9	119.45	
B X C	81	241.36	
A X B X C	81	167.88	

* $P < .025$

TABLE 25

ANALYSIS OF VARIANCE: HR-EXT (All Segments)

Source	df	MS	F
Time Segments (A)	4	3792.05	11.17*
Trials (B)	9	783.01	2.15**
Subjects (C)	9	30104.74	
A X B	36	132.15	0.90
A X C	36	339.36	
B X C	81	363.72	
A X B X C	324	146.08	

* $P \leq .001$ ** $P \leq .05$

TABLE 26

ANALYSIS OF VARIANCE: SV-HAB (All Segments)

Source	df	MS	F
Time Segments (A)	4	13.60	0.60
Trials (B)	4	82.46	1.45
Subjects (C)	4	4607.47	
A X B	16	23.93	1.28
A X C	16	22.65	
B X C	16	56.98	
A X B X C	64	18.74	

TABLE 27

ANALYSIS OF VARIANCE: SV-ACQ (All Segments)

Source	df	MS	F
Time Segments (A)	4	87.62	4.92*
Trials (B)	9	9.20	0.36
Subjects (C)	4	5719.08	
A X B	36	14.53	1.40
A X C	16	17.79	
B X C	36	25.72	
A X B X C	144	10.38	

* $P < .01$

TABLE 28

ANALYSIS OF VARIANCE: SV-ACQ (b, e, 1 Components)

Source	df	MS	F
Time Segments (A)	2	80.66	6.44*
Trials (B)	9	14.11	0.73
Subjects (C)	4	3363.65	
A X B	18	11.33	1.08
A X C	8	12.53	
B X C	36	19.24	
A X B X C	12	10.49	

* $P < .025$

TABLE 29

ANALYSIS OF VARIANCE: SV-EXT (b, e, 1 Components)

Source	df	MS	F
Time Segments (A)	2	70.58	3.00
Trials (B)	9	7.81	0.60
Subjects (C)	4	3355.00	
A X B	18	7.12	0.75
A X C	8	23.52	
B X C	36	13.09	
A X B X C	72	9.48	

TABLE 30

ANALYSIS OF VARIANCE: SV-EXT (All Segments)

Source	df	MS	F
Time Segments (A)	4	77.98	3.36*
Trials (B)	9	17.09	0.84
Subjects (C)	4	5590.53	
A X B	36	7.47	0.73
A X C	16	23.24	
B X C	36	20.24	
A X B X C	144	10.16	

* $P < .05$

TABLE 31

ANALYSIS OF VARIANCE: PR-HAB (All Segments)

Source	df	MS	F
Time Segments (A)	4	43547.72	0.04
Trials (B)	4	2106968.00	1.04
Subjects (C)	3	0.26	
A X B	16	298107.60	1.58
A X C	12	1020129.00	
B X C	12	2034017.00	
A X B X C	48	188726.70	

TABLE 32

ANALYSIS OF VARIANCE: PR-ACQ (All Segments)

Source	df	MS	F
Time Segments (A)	4	1195210.00	2.25
Trials (B)	9	1231417.00	0.52
Subjects (C)	3	.35	
A X B	36	246287.50	1.15
A X C	12	531729.90	
B X C	27	2355692.00	
A X B X C	108	214579.50	

TABLE 33

ANALYSIS OF VARIANCE: PR-ACQ (b, e, 1 Components)

Source	df	MS	F
Time Segments (A)	2	564561.00	3.32
Trials (B)	9	1205748.00	0.65
Subjects (C)	3	0.19	
A X B	18	168278.50	1.36
A X C	6	169871.60	
B X C	27	1854913.00	
A X B X C	54	123443.40	

TABLE 34

ANALYSIS OF VARIANCE: PR-EXT (b, e, l Components)

Source	df	MS	F
Time Segments (A)	2	213278.00	8.04*
Trials (B)	9	89725.12	0.62
Subjects (C)	3	0.18	
A X B	18	67796.00	0.66
A X C	6	265244.00	
B X C	24	144503.40	
A X B X C	54	103054.60	

* $P \leq .025$

TABLE 35

SUMMARY OF RESULTS

<u>Variable</u>	<u>Orienting CR (OCR)</u>	<u>Anticipatory CR (ACR)</u>	<u>Emergence in Acquisition</u>	<u>UCR</u>	<u>Substitutive CR (SCR)</u>	<u>Resistance to Extinction</u>
Coronary Flow	- -	▲	Early (ACR)	▲	Brief & temporary ▲	Minimal (ACR) Moderate (SCR)
Aortic Flow	▲	▲	Late (OCR) Early (ACR)	▲	Brief & temporary ▲	Moderate (OCR & ACR) Minimal (SCR)
Blood Pressure	▲	▲	Early (OCR & ACR)	▲	None	Practically None
Heart Rate	▲	▼	Early (OCR)	▲	None	Extreme (OCR) Minimal (ACR)
Stroke Volume	▼	▲	Middle (OCR & ACR)	Inc.	None	Minimal
Peripheral Resistance	▼	▼	Middle (OCR & ACR)	▲	▲	Maximal

Table 36

Data Reduction

VINCENTIZED TRIALS

P E R I O D		I				II	III	IV	V			
		<u>S#1</u>	<u>S#2</u>	<u>S#3</u>	<u>S#4</u>				<u>S#1</u>	<u>S#2</u>	<u>S#3</u>	<u>S#4</u>
		<u>a</u>	<u>b</u>	<u>c</u>	<u>d</u>				<u>a</u>	<u>b</u>	<u>c</u>	<u>d</u>
		1	1	1	1	.	.	.	60	45	81	37
Baseline		.	.	.	.	.	.	.	.	.	.	.
		.	.	.	.	.	.	.	.	.	.	.
		<u>a</u>	<u>b</u>	<u>c</u>	<u>d</u>	.	.	.	<u>a</u>	<u>b</u>	<u>c</u>	<u>d</u>
		15	11	20	9	.	.	.	75	55	100	45
		$\bar{X}_{a1-1}$	$\bar{X}_{b1-1}$	$\bar{X}_{c1-1}$	$\bar{X}_{d1-1}$	.	.	.	$\bar{X}_{a1-5}$	$\bar{X}_{b1-5}$	$\bar{X}_{c1-5}$	$\bar{X}_{d1-5}$
Reinforcement		<u>S#1</u>	<u>S#2</u>	<u>S#3</u>	<u>S#4</u>				<u>S#1</u>	<u>S#2</u>	<u>S#3</u>	<u>S#4</u>
		<u>a</u>	<u>b</u>	<u>c</u>	<u>d</u>	.	.	.	<u>a</u>	<u>b</u>	<u>c</u>	<u>d</u>
		1	1	1	1	.	.	.	60	45	81	37
		.	.	.	.	.	.	.	.	.	.	.
		.	.	.	.	.	.	.	.	.	.	.
		<u>a</u>	<u>b</u>	<u>c</u>	<u>d</u>	.	.	.	<u>a</u>	<u>b</u>	<u>c</u>	<u>d</u>
		15	11	20	9	.	.	.	75	55	100	45
		$\bar{X}_{a2-1}$	$\bar{X}_{b2-1}$	$\bar{X}_{c2-1}$	$\bar{X}_{d2-1}$	.	.	.	$\bar{X}_{a2-5}$	$\bar{X}_{b2-5}$	$\bar{X}_{c2-5}$	$\bar{X}_{d2-5}$

TABLE 37

Data Analysis

VINCENTIZED TRIALS

P E R I O D		<u>I (B₁)</u>	<u>II (B₂)</u>	<u>III (B₃)</u>	<u>IV (B₄)</u>	<u>V (B₅)</u>
	Baseline (A ₁)	$\bar{X}_{a1-1}$ $\bar{X}_{b1-1}$ $\bar{X}_{c1-1}$ $\bar{X}_{d1-1}$	$\bar{X}_{a1-2}$ $\bar{X}_{b1-2}$ $\bar{X}_{c1-2}$ $\bar{X}_{d1-2}$	$\bar{X}_{a1-3}$ $\bar{X}_{b1-3}$ $\bar{X}_{c1-3}$ $\bar{X}_{d1-3}$	$\bar{X}_{a1-4}$ $\bar{X}_{b1-4}$ $\bar{X}_{c1-4}$ $\bar{X}_{d1-4}$	$\bar{X}_{a1-5}$ $\bar{X}_{b1-5}$ $\bar{X}_{c1-5}$ $\bar{X}_{d1-5}$
		$\bar{X}_{1-1}$	$\bar{X}_{1-2}$	$\bar{X}_{1-3}$	$\bar{X}_{1-4}$	$\bar{X}_{1-5}$
	Reinforcement (A ₂)	$\bar{X}_{a2-1}$ $\bar{X}_{b2-1}$ $\bar{X}_{c2-1}$ $\bar{X}_{d2-1}$	$\bar{X}_{a2-2}$ $\bar{X}_{b2-2}$ $\bar{X}_{c2-2}$ $\bar{X}_{d2-2}$	$\bar{X}_{a2-3}$ $\bar{X}_{b2-3}$ $\bar{X}_{c2-3}$ $\bar{X}_{d2-3}$	$\bar{X}_{a2-4}$ $\bar{X}_{b2-4}$ $\bar{X}_{c2-4}$ $\bar{X}_{d2-4}$	$\bar{X}_{a2-5}$ $\bar{X}_{b2-5}$ $\bar{X}_{c2-5}$ $\bar{X}_{d2-5}$
		$\bar{X}_{2-1}$	$\bar{X}_{2-2}$	$\bar{X}_{2-3}$	$\bar{X}_{2-4}$	$\bar{X}_{2-5}$

TABLE 38

ANALYSIS OF VARIANCE: CORONARY BLOOD FLOW

Source	df	MS	F
Period (A)	1	196.51	12.63*
Trials (B)	4	8.14	0.48
Subjects (C)	3	125.60	
A X B	4	1.87	0.61
A X C	3	15.56	
B X C	12	17.13	
A X B X C	12	3.08	

* $P < .05$

TABLE 39

ANALYSIS OF VARIANCE: HEART RATE

Source	df	MS	F
Period (A)	1	11.02	15.88*
Trials (B)	4	8.24	0.94
Subjects (C)	3	54.29	
A X B	4	0.49	4.29*
A X C	3	0.69	
B X C	12	8.77	
A X B X C	12	0.11	

* $P \leq .05$

TABLE 40

ANALYSIS OF VARIANCE: BLOOD PRESSURE

Source	df	MS	F
Period (A)	1	385.02	2.80
Trials (B)	4	19.16	0.39
Subjects (C)	3	4807.45	
A X B	4	42.79	6.37*
A X C	3	137.54	
B X C	12	49.76	
A X B X C	12	6.72	

* $P < .01$

TABLE 41

TRADITIONAL DISTINCTIONS BETWEEN
RESPONDENT AND OPERANT LEARNING

<u>Operant</u>	<u>Respondent</u>
Control by Contingency	Control by Contiguity
Response is emitted	Response is elicited
Skeletomuscular response	Visceral or glandular response
Motor response	Affective response
Mediated by CNS	Mediated by ANS
Measurement by frequency	Measurement by magnitude, amplitude, or latency
"Voluntary" behavior	"Involuntary" behavior

Table 42. Summary of Animal Studies on Respondent Cardiovascular Conditioning

SPECIES	PARADIGM	CONDITIONED STIMULUS		UNCONDITIONED STIMULUS				
		Type	Duration	Type	Intensity	Duration	Locus	ISI
Goldfish	Delay	Illumination change	3-7 sec	Shock	45 volts	"brief"	diffuse	3-7 sec
Tautog (Blackfish)	Delay	10-500 Hz tone	approx. 11 sec	Shock	.2-.3 ma	.14 sec	dorsal to anal fin	10.86 seconds
Goldfish	Delay	Light	10 sec	Shock	.44, 1.33, 2.22 v, a/c (RMS) /cm	.1 sec	diffuse	10 sec
Lobster	Delay	37.5 Hz tone	10-11 sec	Shock	.2 amps	.14 sec	last pair of legs	10+ sec
Pigeon	Delay-Different.	Light	6.5 sec	Shock	3-7 volts	.5 sec	foot	6 sec
Pigeon	Delay-Different.	Light	6.5 sec	Shock	3-7 volts	.5 sec	foot	6 sec
Pigeon	Delay-Different.	Light	6.5 sec	Shock	3-7 volts	.5 sec	foot	6 sec
Pigeon	Delay-Different.	Light	6.5 sec	Shock	3-7 volts	.5 sec	foot	6 sec
Rabbit	Delay	Bell	5 sec	Ammonia	---	3 sec	nose	---
Rabbit	Delay	1000 Hz tone	2.5 sec	Shock	1.5 ma	.5 sec	ear	2 sec
Rabbit	Trace & Delay Different.	550 Hz tone 3400 Hz tone	0.35 sec 1.00 sec	Shock	3 ma	.3 sec	eyelid	0.35 sec 1.00 sec
Rabbit	Delay-Different.	550 Hz tone 3400 Hz tone	.75, 1.25, 2.75, 7.5 sec	Shock	5 ma	---	eyelid	.25 to 6.75 sec

Table 42 (Cont'd.)										
ITI	CONDITIONED RESPONSE				UNCONDITIONED RESPONSE				IMMOBILIZATION	AUTHORS
	HR	BP	BF	Other	HR	BP	BF	Other		
1-2 min	↓	--	--	RR↓	--	--	--	--	Restraint	Otis, et al (1957)
$\bar{X}$ = 2 min	↓	--	--	--	--	--	--	--	Restraint	Offutt (1971)
$\bar{X}$ = 60 sec	↓	--	--	RR↓	↓	--	--	--	Restraint	Scobie (1973)
--	↓	--	--	--	↓	--	--	--	Restraint	Offutt (1970)
$\bar{X}$ = 7.4 min	↑	--	--	--	↑	--	--	RR↑	Restraint	Cohen & Durkovic (1966)
$\bar{X}$ = 7.4 min	↑	--	--	RR↑	↑	--	--	RR↑	Restraint	Durkovic & Cohen (1969a)
$\bar{X}$ = 7.4 min	↑	--	--	RR↑	↑	--	--	RR↑	Restraint	Durkovic & Cohen (1969b)
$\bar{X}$ = 7.4 min	↑	--	--	RR↑	↑	--	--	RR↑	Restraint	Cohen (1974)
5 min	↑↓	--	--	--	↓	--	--	--	Restraint	Kosupkin & Olmsted (1943)
$\bar{X}$ = 120 sec	↓	--	--	--	Var.	--	--	--	Restraint	Schneiderman, et al (1966)
85 sec	↓	--	--	NM↑	↓	--	--	NM	Restraint	Meredith & Schneiderman (1967)
90 sec	↓	--	--	NM RR	--	--	--	--	Restraint	VanDercar & Schneiderman (1967)

Table 42 (Cont'd.)

SPECIES	PARADIGM	CONDITIONED STIMULUS		UNCONDITIONED STIMULUS			Locus	ISI
		Type	Duration	Type	Intensity	Duration		
Rabbit	Delay	550 Hz tone	4 sec	Shock	20 ma	1 sec	eyelid	4 sec
Rabbit	Delay-Different.	550 Hz tone 3400 Hz tone	.75 sec	Shock	3 ma	.5 sec	eyelid	.25 sec
Rabbit	Delay-Different.	LGN stimulation	2 sec	ESB	1 ma	1 sec	septal & hypothal.	2 sec
Rabbit	Delay-Different.	light flash, tone pips	2.3 sec	Shock	2-9 ma, inc daily	.3 sec	eyelid	2 sec
Rabbit	Delay-Different.	550 Hz tone 3400 Hz tone	.75 sec	Shock	3 ma	.5 sec	eyelid	.75 sec
Rabbit	Delay-Different.	10/sec, 3/sec click trains	35 sec	ESB	.5 ma	15 sec	Septal area	20 sec
Rabbit	Delay-Different.	535 Hz tone 2500 Hz tone	60 sec	ESB	.5 ma	1 sec	septal & hypothal.	60 sec
Rat	Delay	Light	6 sec	Shock	---	.5 sec	feet via grid floor	6 sec
Rat	Delay	12.8/sec click train	5 sec	Shock	.5 ma, 1.5 ma	.3 sec	tail	5 sec
Rat	Delay	1000 Hz tone	7 sec	Shock	1.8 ma	1 sec	rib cage (chest)	6 sec
Rat	Delay	40 dB white noise	.5, 2.5, 5, 10 sec	Shock	1.5 ma	---	feet via grid floor	.5, 2.5, 5, 10 sec
Rat	Delay-Different.	510 Hz tone 1800 Hz tone	90 sec	Shock	1.3 ma	.5 sec	feet via grid floor	90 sec

Table 42 (Cont'd.)										
ITI	CONDITIONED RESPONSE				UNCONDITIONED RESPONSE				IMMOBILIZATION	AUTHORS
	HR	BP	BF	Other	HR	BP	BF	Other		
120 sec	↓	↑	--	RR↑	↓	↑↓	--	RR	Flaxedil or restraint	Yehle, Dauth, & Schneiderman (1967)
120 sec	↓	↑	--	--	↓	↓	--	--	Flaxedil or restraint	Schneiderman, et al (1969)
90 sec	↑	ns	--	--	↓	↑	--	--	Restraint	VanDercar, et al (1970)
---	9%↓	--	--	--	--	--	--	--	?	Yehle, et al (1971)
90 sec	↓	--	--	NM↑ EB↑	--	--	--	--	Restraint	Downs, et al (1972)
2-4 min	--	↓	--	Sharp Inspirat.	--	↓	--	Sharp Inspirat.	Ether Anesthesia	Lico, et al (1968)
4 min	↓	↓	--	--	↓	↓	--	--	Restraint	Sampson, et al (1974)
---	↑↓	--	--	--	↑	--	--	--	None	Bloch-Rojas, et al (1964)
$\bar{X}=2\ 1/2$ min	↓	--	--	GSR↓	--	--	--	--	Restraint	Holdstock & Schwartzbaum (1965)
$\bar{X} = 10$ min	↓	--	--	--	↑	--	--	--	Restraint	Fitzgerald, et al (1966)
$\bar{X} = 2$ min	↑	--	--	--	?	--	--	--	None	Black & Black (1967)
?	↓	--	--	BP ↓	--	--	--	--	None	Parrish (1967)

Table 42 (Cont'd.)

SPECIES	PARADIGM	CONDITIONED STIMULUS		UNCONDITIONED STIMULUS			Locus	ISI
		Type	Duration	Type	Intensity	Duration		
Rat	Delay-Different.	Light	11 sec	Shock	2.4-.... 6.6, 8.0 v.	1 sec	tail	10 sec
Rat	Trace (T) & Delay (D)	1000 Hz tone	1 sec (T) 7 sec (D)	Shock	.4,... 5.0 ma	1 sec	rib cage (chest)	6 sec
Rat	Delay	1000 Hz tone	6 sec	Shock	1.8 ma	1 sec	chest	6 sec
Cat	Delay	1000 Hz tone	4.25 sec	Shock	.7-4.0 ma	.5 sec	right hindfoot	3.5 sec
Cat	Delay-Different.	1000 Hz tone 500 Hz tone	.5 sec	Shock	1.0 ma	5 sec	left foreleg	10 sec
Cat	Trace (T) & Delay (D)	200 Hz tone-T 1000 Hz tone-D	9 sec (T) 2 sec (D)	Shock	.5-4.0 ma	2 sec	right foreleg	7 sec
Cat	Delay-Different.	500 Hz tone 1000 Hz tone	10 sec	Shock	2.5 ma	2 sec	right foreleg	10 sec
Monkey	Delay-Different.	Light	56 sec	Shock	10 ma	.3 sec	neck to buttocks	56 sec
Monkey	Delay-Different.	Lights (complex S ^D)	12 sec	Shock	2 ma	1 sec	ankle to thigh	12 sec
Monkey & Baboon	Delay	Tone	11 sec	Shock	6 ma	1 sec	tail	11 sec
Monkey	Delay	Vertical Line	30.5 sec	Shock	6 ma	300 msec	foot	30 sec
Monkey	Delay	Lights	30 sec	Shock	11 ma	.3 sec	tail	30 sec

Table 42 (Cont'd.)

ITI	CONDITIONED RESPONSE				UNCONDITIONED RESPONSE				IMMOBILIZATION	AUTHORS
	HR	BP	BF	Other	HR	BP	BF	Other		
2 min fixed	↓	--	--	--	↑	--	--	--	Restraint	Tighe, Graves, & Riley (1968)
$\bar{X}$ = 3 min	↓	--	--	--	↑	--	--	--	Restraint	Fitzgerald & Teyler (1970)
$\bar{X}$ = 90 sec	↓	--	--	--	--	--	--	--	Restraint	Phillips & Martin (1972)
2 min fixed	↓	--	--	LF Freezing	--	--	--	--	Hammock restraint	Bruner (1969)
30-90 sec	↓	↓	--	RR apnea Pupil Dil.	↑	↑	--	RR↑, EMG↑ Pupil dil.	None or succinylcholine	Hein (1969)
Approx. 1 min	↓	--	--	RR↓ EMG↑	--	--	--	--	None	Howard, et al (1974)
$\bar{X}$ = 70 sec	↓	--	--	--	↑	--	--	--	3 types of N.M.B.A.'s	Howard, et al (1975)
5, 10, 15 minutes	↑	--	↑	RR	↑	--	↑	RR	Restraint	Smith & Stebbins (1965)
1-3.5 min	↑	--	--	--	↑	--	--	--	Restraint	Miller & Caul (1969)
Up to 35 minutes	↑	↑	--	Epinephrine↑	↑	↑	--	Epinephrine↑	Restraint	Ferreira, Gollub, & Vane (1969)
$\bar{X}$ = 7 min	↑↓	--	--	--	--	--	--	--	Restraint	Ramsay (1970)
2.5 min	↑↓	↑↓	--	--	--	--	--	--	Restraint	Snapper, et al (1971)

Table 42 (Cont'd.)								
SPECIES	PARADIGM	CONDITIONED STIMULUS		UNCONDITIONED STIMULUS			Locus	ISI
		Type	Duration	Type	Intensity	Duration		
Monkey	Delay-Different.	Tones	?	Shock	?	?	tail	?
Monkey	Delay-Different.	3400 Hz tone	60 sec	Shock	1-3 ma	2 sec	abdomen to tail	58 sec
Monkey	Delay-Different.	650 Hz tone 1650 Hz tone	2 sec	Shock	3 ma	0.3 sec	tail	2 sec
Monkey	Delay	Vertical bar	30 sec	Shock	11 ma	0.3 sec	tail	30 sec
Dog	Delay	256, 512, & 1024 Hz tones	5 sec	Shock	1t., med, & intense	0.6 sec	hindleg	4.6 sec
Dog	Delay	256, 512, & 1024 Hz tones	4-6 sec	Shock	1t., med, & intense	0.6 sec	hindleg	4.6 sec
Dog	Delay (D) & Trace (T)	Tone (unspecified)	5 sec (D&T) 23 sec (T&D)	Shock	4.5 ma	3 sec	hind paws	5 sec 20 sec
Dog	Delay	350 Hz tone	13 sec	Shock	9.9 ma	3 sec	rear limbs	10 sec
Dog	Delay	350 Hz tone	13 sec	Shock	9.9 ma	3 sec	rear limbs	10 sec
Dog	Delay	350 Hz tone	13 sec	Shock	9.9 ma	3 sec	rear limbs	10 sec
Dog	Delay?	Tone (unspecified)	?	Shock	?	?	Foreleg	?
Dog	Delay?	Tone (unspecified)	?	Shock	?	?	?	?

Table 42 (Cont'd.)

ITI	CONDITIONED RESPONSE				UNCONDITIONED RESPONSE				IMMOBILIZATION	AUTHORS
	HR	BP	BF	Other	HR	BP	BF	Other		
?	↑	↑	--	↑dp/dt	--	--	--	--	Restraint	Schneiderman, et al (1975)
<u>/</u> 15 min	↑	↑	--	↑dp/dt	↑	↑	--	↑dp/dt	Restraint	Randall, Brady, & Martin (1975)
90 sec	↑	↑	--	--	↑	↑	--	--	Restraint	Klose, et al (1975)
4-16 min	↑	--	--	--	--	--	--	--	Restraint	Pomerleau, et al (1969)
2 min	↑	--	--	LF↑	↑	--	--	LF↑	Semi-restraint	Dykman, et al (1956)
2 min	↑	--	--	LF↑	↑	--	--	LF↑	Semi-restraint	Dykman & Gantt (1958)
3 min	↑	--	--	--	--	--	--	--	Hammock restraint	Church & Black (1958)
$\bar{X}$ = 3.5 min	↑	--	--	R ampl.	--	--	--	--	?	Fitzgerald & Wallach (1966)
$\bar{X}$ = 3.5 min	↑	--	--	--	↑	--	--	--	Restraint	Fitzgerald (1966)
$\bar{X}$ = 3.5 min	↑	--	--	--	↑	--	--	--	Restraint	Fitzgerald, et al (1966)
?	4↑ 3↓	↑↓	--	EMG variable	--	--	--	--	Succinylchol. & d-Tubocur.	Newton (1967)
?	↑	↑	--	RVP↑ SV↓	--	--	--	--	?	Perez-Cruet & Gaertner (1967)

Table 42 (Cont'd.)

SPECIES	PARADIGM	CONDITIONED STIMULUS		UNCONDITIONED STIMULUS				ISI
		Type	Duration	Type	Intensity	Duration	Locus	
Dog	Delay-Different.	480 Hz tone 1000 Hz tone	10 sec	Shock	800 Hz DC	1 sec	foreleg	10 sec
Dog	Delay-Different.	150 Hz tone 1200 Hz tone	15 sec	Shock	.5-6.0 ma	5 sec	hindleg footpads	10 sec
Dog	Delay	480 Hz tone	11 sec	Shock	approx. 3-5 ma	1 sec	footpad	10 sec
Dog	Delay?	Tone (unspecified)	?	Shock	unspec.	--	--	7 sec
Dog	Trace	Whistle	brief	Shock	unspec.	1 sec	foot	2 sec
Dog	Delay-Different.	5 diff. tones	10 sec	Shock	.8-1.2 ma	0.5 sec	foreleg	10 sec
Dog	Delay	1000 Hz tone	7 sec	Shock	1-5 ma	2 sec	left foreleg	7 sec

Table 42 (cont'd)

ITI	CONDITIONED RESPONSE				UNCONDITIONED RESPONSE				IMMOBILIZATION	AUTHORS
	HR	BP	BF	Other	HR	BP	BF	Other		
55 sec	↑	--	--	--	--	--	--	--	Restraint vs free	Pare (1967)
$\bar{X}$ = 60 sec	↑	--	--	--	↑	--	--	--	Hammock with d-Tubocurare	Church, et al (1966)
$\bar{X}$ = 2 min	↑	--	--	↓HR var.	--	--	--	--	?	Lynch (1968)
?	↑	--	--	--	--	--	--	--	?	Howard, et al (1970)
30-90 sec	↑	↓	↑	LF	↑	↓	↑	LF	Harness	Antal & Gantt (1970)
?	↑	↑	--	--	--	--	--	--	Harness	Kakigi (1971)
60-90 sec	↑	↑	--	↑contract- ility	↑	↑	--	↑contract- ility	Restraint	Obrist, et al (1972)

Figure Captions

Figure 1. Mean coronary flow response of eight dogs during habituation and acquisition (b = baseline, e = early CS, l = late CS, u = UCS period, p = post-stimulus interval; ○ = baseline & post-stimulus intervals, ● = CS only, ▲ = UCS).

Figure 2. Mean coronary flow response of eight dogs during extinction (b = baseline, e = early CS, l = late CS, u = UCS period, p = post-stimulus interval; ○ = baseline & post-stimulus intervals, ● = CS only).

Figure 3. Mean aortic flow response of five dogs during habituation and acquisition (b = baseline, e = early CS, l = late CS, u = UCS period, p = post-stimulus interval, ○ = baseline & post-stimulus intervals, ● = CS only, ▲ = UCS).

Figure 4. Mean aortic flow response of five dogs during extinction (b = baseline, e = early CS, l = late CS, u = UCS period, p = post-stimulus interval; ○ = baseline & post-stimulus intervals, ● = CS only).

Figure 5. Mean blood pressure response of ten dogs during habituation and acquisition (b = baseline, e = early CS, l = late CS, u = UCS period, p = post-stimulus interval; ○ = baseline & post-stimulus intervals, ● = CS only, ▲ = UCS).

Figure 6. Mean blood pressure response of ten dogs

during extinction (b = baseline, e = early CS, l = late CS, u = UCS period, p = post-stimulus interval; ○ = baseline & post-stimulus intervals, ● = CS only).

Figure 7. Mean heart rate response of ten dogs during habituation and acquisition (b = baseline, e = early CS, l = late CS, u = UCS period, p = post-stimulus interval; ○ = baseline & post-stimulus intervals, ● = CS only, ▲ = UCS).

Figure 8. Mean heart rate response of ten dogs during extinction (b = baseline, e = early CS, l = late CS, u = UCS period, p = post-stimulus interval; ○ = baseline & post-stimulus interval, ● = CS only).

Figure 9. Mean stroke volume response of five dogs during habituation and acquisition (b = baseline, e = early CS, l = late CS, u = UCS period, p = post-stimulus interval; ○ = baseline & post-stimulus intervals, ● = CS only, ▲ = UCS).

Figure 10. Mean stroke volume response of five dogs during extinction (b = baseline, e = early CS, l = late CS, u = UCS period, p = post-stimulus interval; ○ = baseline & post-stimulus intervals, ● = CS only).

Figure 11. Mean peripheral resistance response of four dogs during habituation and acquisition (b = baseline, e = early CS, l = late CS, u = UCS period, p = post-stimulus interval; ○ = baseline & post-stimulus intervals, ● = CS only, ▲ = UCS).

Figure 12. Mean peripheral resistance response of four dogs during extinction (b = baseline, e = early CS, l = late CS, u = UCS period, p = post-stimulus interval; ○ = baseline & post-stimulus intervals, ● = CS only, ▲ = UCS).

Figure 13. Correlation coefficients of coronary flow with other direct measures for the 30-sec. stimulus interval across habituation, acquisition, and extinction.

Figure 14. Correlation coefficients of coronary flow with derived measures for the 30-sec. stimulus interval across habituation, acquisition, and extinction.

Figure 15. Mean per cent change in coronary blood flow (CF) and corresponding changes in heart rate (HR), aortic blood flow (AF), and blood pressure (BP) across Vincentized segments of operant acquisition for a typical subject (BF7).

Figure 16. Mean per cent change in coronary blood flow (CF) and corresponding changes in heart rate (HR) and blood pressure (BP) across Vincentized segments of operant acquisition for a particularly responsive subject (BF39).

Figure 17. Polygraph record of a sample trial from a particularly responsive subject depicting late acquisition (CF = coronary blood flow, HR = heart rate, BP = blood pressure, CS = conditioned stimulus, UCS = unconditioned stimulus).

Figure 18. Mean per cent change in coronary blood flow (CF) and corresponding changes in heart rate (HR) and blood pressure (BP) across Vincentized segments of operant acquisition for grouped subjects.

Figure 19. Mean coronary blood flow of four subjects at baseline (B) and reinforcement (R) periods across Vincentized segments of operant acquisition.

Figure 20. Corresponding mean heart rate of four subjects at baseline (B) and reinforcement (R) periods across Vincentized segments of operant acquisition.

Figure 21. Corresponding mean blood pressure of four subjects at baseline (B) and reinforcement (R) periods across Vincentized segments of operant acquisition.

Figure 22. Mean latencies and per cent avoidance responses across Vincentized segments of operant acquisition for grouped subjects trained to decrease coronary blood flow.

Figure 23. Latencies of criterion increases in mean coronary blood flow reflecting learned avoidance across 55 trials (Ra = avoidance responses).

Figure 24. Mean latencies of criterion increases in coronary blood flow reflecting learned avoidance across blocks of five trials.

Figure 25. Polygraph record of operant training of increases in coronary blood flow , trial #1 (H.R. = heart rate, C.F. = coronary blood flow, A.F. = aortic blood flow, B.P. =

blood pressure, CS = conditioned stimulus, UCS = unconditioned stimulus).

Figure 26. Mean per cent change in coronary blood flow (CF) and corresponding changes in aortic blood flow (AF), blood pressure (BP), and heart rate (HR) across Vincentized segments of operant acquisition for a subject trained to increase coronary flow after decrease training.

Figure 27. The circulatory system.

Figure 28. Cardiovascular electrical and mechanical events.

Figure 29. Factors influencing coronary blood flow.

FIGURE 1

FIGURE 2

FIGURE 3

FIGURE 4

FIGURE 5

FIGURE 6

FIGURE 7

FIGURE 8

FIGURE 9

FIGURE 10

FIGURE 11

FIGURE 12

FIGURE 13

FIGURE 14

Figure 15.

Figure 16.

Figure 17.

Figure 18.

Figure 19.

Figure 20.

Figure 21.

Figure 22.

APPENDIX A

OPERANT CONTROL OF INCREASES IN CORONARY

BLOOD FLOW: PRELIMINARY DATA

As indicated earlier, any attempt to operantly condition increases in coronary blood flow using the stress reduction reinforcement of the escape-avoidance paradigm is clearly confounded by the stress-induced increase in coronary blood flow which is naturally elicited by the aversive respondent characteristics intrinsic to the escape-avoidance arrangement of stimuli. Miller's group (Miller, 1969) offered between-subject bi-directional conditioning as the primary control procedure for this type of confounding but the between-subject bi-directional control is half illusory and half substantive. It is substantive only in that half of the procedure involves conditioning the subject to emit responses which mitigate against respondently elicited antagonistic behavior. It is illusory in that operant shaping of responses in the same direction as the respondently elicited changes have rarely been shown to exceed the magnitude of the respondent CR. Indeed, if the magnitude of a respondent CR can be improved with practice using this type of procedure, there is nothing in the procedure to differentiate the affect of the contingency from the simple improvement in the respondent CR by virtue of additional acquisition trials! In this important respect the latter half of the bi-directional

control is unnecessary if not entirely misleading.

There are, however, two important alternatives to the between-subject bi-directional control procedure: a) the fixed-criterion escape-avoidance paradigm, and b) the within-subject sequentially shaped bi-directional operant procedure.

Fixed-Criterion Escape-Avoidance Training. The first of these procedures was attempted with one subject in the present study. This animal had been subjected to respondent habituation, acquisition, and extinction in a previous session. In this second session he was returned for fixed-criterion escape-avoidance training. A contingency was programmed in which the subject was required to consistently increase baseline coronary blood flow of 116-146 cc/min to a mean of 225 cc/min in order to escape from or avoid shock. Figure 23 illustrates the latencies to criterion across each of 55 trials. This figure clearly demonstrates the improvement in the ease with which the response is performed. Only 1/3 of the first 15 responses avoid the onset of shock while 87% of the last 15 are instrumental in avoiding shock. Figure 24 presents the acquisition of avoidance by blocks of five trials. Most notably, the form of this curve is very similar to that which is commonly seen in the laboratory demonstration of motor escape-avoidance conditioning with rats.

This procedure is subject to one criticism. In particular, it might be argued that the decrease in the latency of the criterion change in coronary flow might only reflect an enhancement or facilitation of the respondent response to the associative features of the training procedure. In this important respect the control procedure is confounded. However, interestingly, the author has never found this criticism directed to the bar-press escape-avoidance procedures so frequently reported in the literature. Yet the only difference is the nature of the learned response: i.e., visceral versus motor.

Within-Subject Bi-Directional Control. The most powerful control for respondent confounding of conditioning by escape-avoidance training is the procedure by which the operant target is antagonistic to the naturally occurring respondent. This procedure also provides the basis upon which confounding is removed from the operant control of increases in coronary blood flow when escape-avoidance training is employed. That is, once the respondent increase in coronary flow has been replaced by the operantly shaped decrease, the respondent artifact is resultingly eliminated. Indeed, the artifact is more than eliminated. The stimuli now are associated with, and elicit, changes that mitigate against the new operant target. As a consequence, a strong argument can be made for the assertion that the effect is the unbiased result of manipulating a

contingency rather than that of simple association.

This procedure was employed with one animal who had survived a previous session of respondent habituation, acquisition, and extinction and a session of operant decreases in coronary blood flow. Figure 25 illustrates the first attempt (trial #1) to shape increases in coronary blood flow in an animal who had learned to emit decreases for the same reinforcement. Of particular interest in this figure is the appearance of two emitted decreases which carry over from the previous training session. Neither is reinforced, and indeed the second decrease is punished with the onset of shock. With shaping, an increase in blood flow is gradually re-developed until the animal is regularly emitting 15-25% increases in order to escape from and avoid shock. Figure 26 illustrates the Vincentized re-acquisition of the coronary increase over a total of 26 trials. The accompanying changes in aortic flow, blood pressure, and heart rate are also included. It is difficult to interpret the influence of the accompanying cardiovascular changes on the basis of the relatively small number of trials available for analysis. In any event, it seems abundantly clear that an increase in coronary blood flow has been shaped using the same reinforcement which previously shaped and strengthened a response in the opposite direction.

Figure 23.

Figure 24.

Figure 25

Figure 26.

APPENDIX B

CARDIOVASCULAR DYNAMICS AND CORONARY CIRCULATION

The cardiovascular system consists of the heart and blood vessels whose primary function is to circulate blood throughout the body so that 1) oxygen and other nutrients can be applied to the tissues, and 2) tissues can release carbon dioxide, metabolites and other wastes which are created as by-products of energy expenditure¹. The heart is essentially a four-chambered "double pump" in this system which maintains a pressure gradient through a network of elastic tubes which complete a circle of flow from the left to the right side of the pump. This arrangement is described in Figure 27 which illustrates the movement of blood from the left ventricle through the aorta where it is distributed to the tissues via a system of large systemic arteries which bifurcate into smaller arteries and arterioles finally reaching the capillary level where the exchange of nutrients and gases occurs. Blood is returned to the right half of the heart through the venules, small to large veins, the vena cava caudalis, right atrium and right ventricle (right half of the pump) which returns blood to the left ventricle by the way of the pulmonary circulation where reoxygenation is achieved.

The hearts pumping action has electrical and mechanical characteristics which interrelate with other

cardiovascular events as depicted in Figure 28. Each cardiac cycle can be represented electrically by voltage fluctuations as seen in the electrocardiogram (ECG). The cycle begins with atrial excitation shown as a P-wave in the ECG. Atrial contraction immediately follows the P-wave filling the right and left ventricles. Actually ventricular filling is determined as much by the lowered pressure of the relaxed ventricle (a type of sucking action) as by the push of blood by the pumping action of the atria. The QRS complex represents ventricular excitation after which mechanical contraction ensues forcing blood from the left ventricle through the aortic valve into the aorta toward the peripheral systemic circulation and from the right ventricle through the pulmonary artery to the lungs. The T-wave represents ventricular re-polarization and has no mechanical parallel. Atrial repolarization has no electrical representation in the ECG although it is thought to be masked by the QRS complex.

An average cardiac cycle takes about 800 msec during which the atria contract in approximately 100 msec and ventricles contract for 300 msec (systole). The remaining 400 msec allows for rest and re-filling of the chambers. It is during this "rest period" or diastole that most of the coronary flow is allowed to progress as the result of the decrease in intramyocardial tension.

Blood pressure in the cardiovascular system is maintained by two primary and three secondary factors. Cardiac output (CO) is the first primary factor and is determined by the volume of blood pumped per minute by one ventricle which is the product of two factors: a) stroke rate, and b) stroke volume. CO is a simple multiplicative function of these two factors expressed in ml/min. Peripheral resistance is the second primary factor. This is determined simply by the change in the diameter of small peripheral arteries and arterioles. This mechanism is mediated by the vessels in a spiral fashion. Blood pressure is the simple product of cardiac output and peripheral resistance.

Three secondary factors also influence blood pressure:

- a) The elasticity of the large arteries near the heart. For example, with increasing age the arterial walls become more rigid and this rigidity causes increased pressure as the result of increased resistance to blood flow.
- b) The viscosity of the blood. As the blood is more viscous, pressure in the circulatory system increases because of the increased demands on the driving pressure.
- And c) The volume of blood on the system. Obviously, the greater the volume of blood in the system, the more there is additional pressure created in general.

Coronary Circulation

The heart requires proportionally a much greater blood supply than any other organ of the body. This is partly due

to the fact that muscle tissue and other organs extract only 10-25% of circulating oxygen while the heart uses 80%. It manifests almost completely aerobic energy metabolism unlike skeletal muscle.

The heart receives this blood supply through two coronary arteries which are the first to leave the aorta. The right coronary artery descends over the anterior surface of the right ventricle terminating near the apex, posterior surface of the right ventricle, and penetrating the interventricular septum. The left coronary artery bifurcates close to its origin into the left anterior descending branch and the left circumflex branch. The anterior and posterior surfaces of the left ventricle, part of the apex, and most of the interventricular septum are fed through these two branches of the left coronary artery.

There are four primary factors which determine coronary blood flow: 1) hydraulic or mechanical cardiovascular determinants, 2) myocardial metabolism, 3) autonomic nervous influence, and 4) neurohumoral action. As Feigl points out, the influence of any one of these factors is rather easily understood. However, their interaction is extremely complex and in some cases not fully understood.

Mechanical Factors. The hydraulic or cardiovascular mechanical determinants are presented in Figure 29. (Resistance is minimal in right ventricular myocardium and therefore right coronary flow differs markedly from left coronary

flow in this respect.) Left ventricular coronary blood flow occurs primarily during diastole. This is determined by changes in intramyocardial resistance during systolic and diastolic phases. Left coronary flow is terminated during systole because of increased intramyocardial compression. Indeed there is actually a brief period of negative or backflow (more accurately, retrograde flow) during maximal systolic-related compression. Therefore any change in the compression of intramyocardial tissue increases resistance at arteriolar, arterial, and collateral levels directly affecting coronary flow. Consequently, systolic rate and duration determine diastolic time during which the coronaries fill. Coronary perfusion pressure determines the rate at which the coronaries fill in diastole and this pressure is directly affected by aortic pressure changes.

Metabolic Factors. The most urgent stimulus to, and therefore the most pervasive influence on coronary flow is myocardial oxygen consumption. A deficit in myocardial oxygen induces an immediate coronary vasodilation. With all other factors held constant, the coronary system can dilate to a degree sufficient to increase flow by as much as five times baseline. The primary mechanism of this increased flow appears to be at the arteriolar level. It has been postulated that this profoundly dynamic potential is mediated by the breakdown of chemical byproducts to

adenosine which acts directly on arteriolar smooth muscle as a powerful vasodilator.

In the normal heart, oxygen consumption is influenced by a number of cardiovascular events which therefore secondarily affect coronary blood flow. For example, tachycardia increases oxygen consumption and the need for coronary flow; however, decreased diastolic time limits the duration of coronary filling. Increased cardiac volume and size results in increased work particularly where aortic pressure and/or peripheral resistance are maximal. The consequence is increased myocardial oxygen consumption and hence an increase in coronary flow demands. The velocity of cardiac fiber shortening is yet another indirect mechanical influence although its influence on oxygen consumption is least understood compared to other factors. However, with increased sympathetic or catecholamine stimulation, stroke volume is maintained or increased at unchanged end-diastolic cardiac size thus increasing contraction velocity which is suspected to influence oxygen consumption and therefore coronary flow demands.

Autonomic Influence. The coronary system is richly innervated by the sympathetic and parasympathetic divisions of the autonomic nervous system. However, the heart and other blood vessels are also innervated similarly and it is often difficult to determine whether or not the action on coronary vasomotor activity is direct or secondary to

autonomic control of the rest of the cardiovascular system. For example, stimulation of the stellate ganglion causes increased heart rate, aortic pressure, and more vigorous myocardial contractility. These changes induce an increase in myocardial oxygen consumption and a secondary increase in coronary vasodilation.

Under controlled experimental conditions, however, specific aspects of autonomically-mediated coronary changes can be demonstrated. The positive inotropic (force, velocity) and chronotropic (rate) effects of sympathetic stimulation can be blocked by the administration of the drug, propranolol, which is a beta-adrenergic blocking agent. Under these circumstances stellate ganglion stimulation results in consistent coronary vasoconstriction indicating that the direct sympathetic influence on the coronaries is vasoconstriction. This vasoconstriction is mediated by alpha-adrenergic receptors since the response is blocked by phentolamine, an alpha blocker. Beta-adrenergic coronary vasodilation has been demonstrated pharmacologically with isoproterenol but this receptor mechanism has not been as firmly established as the alpha-adrenergic system.

Parasympathetic control of coronary vasomotor activity has been demonstrated by vagal stimulation. However, in the intact preparation this coronary flow decrease is secondary to vagally-induced bradycardia, systemic hypotension, and decreased myocardial metabolism. When

bradycardia is prevented by cardiac pacing, a clear coronary vasodilation is demonstrated by vagal stimulation.

Neurohumoral Influence. Norepinephrine is a primary coronary vasoconstrictor, however, the action of this catecholamine on the mechanical activity of the heart causes vasodilation secondary to increased oxygen demands. Epinephrine also has a secondary vasodilatory action while pitressin (vasopressin) has a profound vasoconstrictor influence on the coronary system. In general, catecholamines have a general influence on often several mechanical variables thereby affecting the all-important oxygen consumption factor and secondarily influencing coronary blood flow.

Figure 27 The Circulatory System (Adapted from Attinger, 1971)

Figure 28 Cardiovascular electrical and mechanical events

Figure 29. Factors Influencing Coronary Flow³

APPENDIX C

AVERSIVE RESPONDENT CONDITIONING OF CARDIOVASCULAR FUNCTION

PROCEDURAL VARIATIONS

Several hear-rate (HR) conditioning studies have employed many procedural variations of the respondent paradigm with every conceivable laboratory species from goldfish to man, only to discover wide between-species variation in results. The primary procedural differences between studies involve slight variations in the following six variables:

1. Type of conditioning paradigm
 - a. Delay
 - b. Trace
 - c. Differentiation
2. Conditioned stimulus (CS) characteristics
 - a. Type
 - b. Duration
3. Unconditioned stimulus (UCS) characteristics
 - a. Type
 - b. Intensity
 - c. Duration
 - d. Locus
4. Interstimulus Intervals (ISI)
5. Intertrial Intervals (ITI)
6. Type of immobilization
 - a. Harness restraint
 - b. Hammock restraint
 - c. Semi-restraint (leash)
 - d. Restraint (apparatus)
 - e. Anesthesia
 - f. Neuro-muscular blocking agents

1. Flaxedil
2. Succinylcholine chloride
3. d-tubocurarine chloride
4. d-tubocurarine iodide

Of these six variables, the types of conditioning paradigms are perhaps most in need of being described in further detail to facilitate the readability of the review which follows. The most commonly-employed paradigm is the delay procedure in which the CS and UCS are presented in the following temporal arrangements:

For the delay procedure, the CS and UCS always either overlap and terminate simultaneously or the UCS onset is simultaneous with the CS offset. In the trace paradigm, the CS offset always precedes the onset of the UCS as follows:

This arrangement is a less effective conditioning procedure and is therefore not commonly used. Finally, very often a differentiation procedure is used as a control for sensitization. Differentiation involves the use of two stimuli,

one of which is systematically followed by the UCS and the other of which is never followed by the UCS. The differentiation procedure can be employed with a delay arrangement (delay-differentiation) or a trace arrangement (trace-differentiation). In either case, respondent acquisition is expected to develop to the reinforced stimulus (CS+) and not to the other stimulus (CS-).

In the following review of cardiovascular conditioning all of the germain studies will be described and summarized for each laboratory species since most of the discrepancies in results can be accounted for on the basis of between-species differences, particularly for heart-rate (HR) conditioning. Speculation will also be entertained relative to the potential sources of variation in results between two groups of species; those which are prone to "freezing" as a component of fear, and those more prone to immediate "flight". Finally, all of the studies are described by species, procedural variations, and results in the chart at the end of this appendix.

HR Conditioning by Species

FISH & LOBSTER. There have been at least three studies of cardiovascular aversive conditioning in the fish and the findings appear quite consistent. The earliest was by Otis, Cerf, & Thomas (1957) who employed a change in illumination (CS) and shock administered diffusely to goldfish while they were immobilized by a restraint technique. They

discovered that a HR decelerative CR was accompanied by an inhibition of respiration. In a similar study, Scobie (1973) more systematically investigated conditioned cardiovascular responses in the same species and also found HR and respiratory decelerative CR's. Offut (1970, 1971) attempted to chart auditory thresholds in the tautog (blackfish) and the American lobster (*Homarus americanus*) by employing an aversive respondent paradigm. In so doing, he firmly established HR decelerative CR's as common to both species.

PIGEON. The only other non-mammalian species in which aversive cardiovascular conditioning has been studied is the pigeon. Virtually all of the work with pigeons has been in the same laboratory (Cohen & Durkovic, 1966; Durkovic & Cohen, 1969a; Durkovic & Cohen, 1969b; Cohen, 1974) and again findings appear to be reasonably consistent for the species. In three of the studies an identical delay-differentiation paradigm was employed in which shock was paired with one color light CS and not with another color. Increases of both HR and respiration rate were conditioned to the shock-paired light in each of the studies but, in one, a bi-phasic HR increase/decrease was found for some birds while others manifested a simple monophasic increase. In the more recent study (Cohen, 1974), conditioned HR increases were shown to be enhanced by increasing the CS intensity. Cohen argues that a sensitization

phenomenon appears to be responsible for the enhancement since sensitization control pigeons reflected similar changes. Consequently, he asserts that performance (sensitized changes in behavior) is selectively affected rather than conditioning (learned changes in behavior) per se. In any event, aversively conditioned HR acceleration appears to be a rather conclusive finding for the species.

RABBIT. One of the earliest studies with mammals in which aversive cardiovascular conditioning was attempted appeared in 1943. In an anecdotal report, Kosupkin & Olmsted (1943) investigated the HR response in the rabbit using ammonia as a UCS and a 5-sec. bell as a CS. The UCR to the inhalation of ammonia for the rabbit is a profound bradycardia of from a 225 bpm baseline to approximately 55 bpm. Within a few pairings of the CS and UCS the authors found a 30-36 bpm decelerative CR for five animals.

More recently Schneiderman and his colleagues have investigated aversive cardiovascular condition quite comprehensively using rabbits as subjects. In their earlier report (Schneiderman, Smith, Smith, & Gormezano, 1966) HR deceleration to a 1000 Hz tone was found to occur within 10 CS-UCS pairings. The UCR was not consistent for all animals but often slight HR acceleration was noted upon repeated UCS presentations. In this respect the results differ from the ammonia study in an important way. Ammonia elicited a profound bradycardia and the CS was ultimately

to elicit "a fraction of that response". With a shock as the UCS, the CS often elicits a response wholly dissimilar to the UCR, and indeed, opposite in direction. For example, as will be seen later, the UCR to shock for rats and cats is HR acceleration. However, the CR for these two species is consistently deceleratory. In further studies with rabbits Meredith & Schneiderman (1967) studied two different interstimulus interval (ISI) durations in both a trace and delay differentiation paradigm. Deceleration of HR to the CS was the consistent finding and the magnitude of the decelerative response appeared to be enhanced by a longer ISI. In an extension of this work, Vandercar & Schneiderman (1967) employed additional ISI durations in a delay differentiation paradigm and found that a 2.25 sec. interval was more effective in conditioning HR deceleration than were 0.25, 0.75, and 6.75 sec. intervals. Once again, the CR was a deceleration of HR which was replicated for the rabbit irrespective of the paradigm. Yehle, Lai, and Sheu (1971) demonstrated that a fixed-criterion (9%) decelerative HR CR could be maintained in the rabbit for up to 40 sessions by gradually increasing the shock UCS over a range of 1 to 10+ ma.

Yehle, Douth, & Schneiderman (1967) examined the decelerative HR CR in the rabbit under two circumstances of relative immobilization: restraint and Flaxedil (gallamine triethiodide). In addition, blood pressure (BP) and

respiration rate were monitored. A simple delay paradigm was employed with 45 tone-shock pairings. Results indicated that responsively conditioned HR deceleration could well have been a "compensatory response to sympathetically induced elevations in arterial blood pressure" and that conditioned BP increases were attenuated by baseline elevations induced by administration of Flaxedil. However, while HR and BP were intimately tied during UCS's, they often appeared to uncouple during CS's, particularly later acquisition. In addition, acceleratory CR's accompanied HR and BP changes during the CS.

Schneiderman, VanDercar, Yehle, Manning, Golden, & Schneiderman (1969) investigated the effects of alpha adrenergic and cholinergic blockade on the form of the HR and BP responses to tone CS's and shock UCS's. Again they found that BP increases may contribute to HR deceleration but that the relationship is not perfect. Injections of Hydergine, an alpha adrenergic blocker, decreased baseline BP's and had a corresponding impact on HR UCRs. Interestingly, however, no animals manifested BP CR's in spite of the fact that all revealed significant BP increase UCR's. Differentiated HR decelerative CRs developed in a control and unilateral vagotomy group but not in bilateral vagotomy, Flaxedil, Hydergine, and atropine treated groups. It was argued that Hydergine interfered with conditioning indirectly by its dampening of BP responses while atropine and

Flaxedil interfered with vagal function, as of course would the bilateral vagotomy. A further test of the atropine effects was performed by Downs, Cardozo, Schneiderman, Yehle, VanDercar, & Zwillling (1972) who found that 10 mg/kg doses of atropine reduced but did not eliminate HR decelerative CR's while doses of 18 mg/kg and 26 mg/kg abolished them. Nictitating membrane response, however, was not adversely affected by any doses of the drug.

In summary, it appears that HR aversive respondent CR's for the rabbit are patently decelerative and probably vagally mediated. The HR response may or may not be tied to conditioned BP increases and are in fact less likely to as acquisition progresses. It is possible that CNS control via the lateral hypothalamus and septal area is also of potential importance in the conditioning of cardiovascular behavior since several investigators have demonstrated a profound impact on HR and BP through electrical stimulation of these areas (VanDercar, Elster, & Schneiderman, 1970; Powell, Goldberg, Dauth, Schneiderman, and Schneiderman, 1972; Lico, Hoffman, & Covian, 1968; Sampson, Francis, & Schneiderman, 1974). However, the results of these brain stimulation studies have not been entirely consistent, reflecting both increases and decreases in HR and BP to the same site of stimulation.

RAT. Another species for which there appears to be reasonable consistency in the literature is the rat. Block-

Rojas, Toro, & Pinto-Hamuy (1964) demonstrated that HR acceleration was invariably the UCR to shock but that the CR was accelerative for some Ss and decelerative for others. In neodecorticate rats, however, orienting HR responses were diminished and HR decelerative CRs were more frequent which perhaps implicates the neocortex as a mediator of vagal inhibition.

In the only inconsistent report on HR conditioning with rats, Black & Black (1967) found HR decelerative CR's in early acquisition trials followed by HR accelerative CR's of 5-40 bpm on subsequent trials. Furthermore HR conditioning was not as effective for extreme (0.5 sec. and 20 sec.) interstimulus intervals (ISI) as it was for intermediate ISI's (2.5 and 5 secs.).

The remainder of studies in which rats were used reflect a consistent finding of decelerative HR responses to aversive CSs. Fitzgerald, Vardaris, & Brown (1966) reported unconditioned acceleration and conditioned deceleration which was not affected by a 100% versus 50% reinforcement schedule. Parrish (1967) employed a combination delay-differentiation/Conditioned Emotional Response (CER) paradigm to study HR concomitants of bar press suppression. He found consistent decelerative CR's accompanying bar-press suppression. Interestingly, his data also reflected the acquisition of a significant HR increase to the non-reinforced stimulus suggesting a disinhibitory phenomenon

of perhaps a vagal origin.

Holdstock & Schwartzbaum (1965) compared two shock intensities in a delay paradigm versus a pseudoconditioning procedure in which the shock followed a click-train CS at randomly determined intervals ranging from 30 to 75 seconds but was never paired with the CS. HR deceleration was evident for both shock intensities in the delay paradigm and HR acceleration was characteristic of pseudoconditioning subjects. Decreased galvanic skin resistance was also conditioned along with a "freezing" response as measured by EMG activity in the thigh muscle. Tighe, Graves, & Riley (1968) also found unconditioned HR acceleration and conditioned deceleration in which a delay-differentiation paradigm was employed. Successive reversals of the reinforced and nonreinforced stimuli generated a learning curve quite similar to successive reversals of discrete motor response operant discriminations.

Fitzgerald and Teyler (1970) investigated HR conditioning in the rat in which a trace was compared with a delay paradigm, and within those conditions, UCS intensities were manipulated. All combinations of procedures reflected accelerative HR UCRs and decelerative CRs. However, the delay paradigm was superior to the trace paradigm in both magnitude and rapidity of acquisition. UCS intensity affected trace acquisition in a positive monotonic fashion while the delay procedure reflected an inverted-U shaped

function of increasing shock intensity. Finally, Phillips & Martin (1972) confirmed decelerative HR CR's for rats and found that the destruction of olfactory input by lesion and nerve section does not affect SS acquisition of the response.

For the rat too, then, there does appear to be sufficient consistency to conclude that HR acceleration is common to the receipt of an aversive stimulus and deceleration is the aversive respondently conditioned response for the species. It is not clear from the methodology reported by Black & Black (1967) described above why they were unable to replicate this consistent finding.

CAT. There have been very few studies in which cats have been used as subjects. Nonetheless, one of the more elegant studies of cardiovascular conditioning was by Hein (1969) who measured several autonomically mediated functions in an aversive respondent study with cats in which a delay-differentiation paradigm was employed. He found a highly consistent set of responses which emerged with regularity particularly in advanced acquisition. Of specific relevance to the present review, HR increased to shock and decreased to the differentially reinforced CS. Hein proposes that vagal influence probably is significant but that it fails to account for the regular complex set of visceral and glandular responses which accompanied HR changes which include pupil dilation, respiratory apnea,

blood pressure (BP) decrease, and decreases in EMG.

Howard, Obrist, Gaebeline, & Galosy (1974) also employed multiple dependent measures in two aversive respondent experiments in which first a trace and then a delay procedure were studied. Of the four subjects in the trace condition, two manifest monophasic decelerative HR CRs and two showed biphasic increase to decrease HR CRs. These deceleratory CRs were accompanied by correlated decreases in general activity. Changes in respiratory amplitude and nuchal EMG were also correlated with the direction of HR change but less consistently so. In the delay procedure, a measure of EEG activity in the pyramidal motor tract at the level of the medullary pyramids was also included. The CR was once again HR deceleration and while general activity and activity in the pyramidal motor tract also decreased simultaneously, there was no correlated change in nuchal muscle EMG.

Bruner (1969), in a leg-flexion study with cats, noted that all of his subjects developed reliable HR decelerative CRs which proved to correlate well with "freezing". Also, flexion CRs developed only in those cats who first manifest HR deceleration and freezing. The UCR to shock was consistently HR acceleration.

In a more recent study Howard, Gaebeline, Galosy, & Obrist (1975) investigated the impact of three neuromuscular blocking agents on autonomic control of heart rate and

blood pressure in cats. An aversive respondent conditioning study in which a delay-differentiation procedure was employed compared d-tubocurarine chloride, dimethyl d-tubocurarine iodide, and succinylcholine chloride with a saline control. The first phase of this study investigated the impact of each of these drugs on HR, BP, and EMG during baseline conditions, sympathetic stimulation (right stellate ganglion), and vagal stimulation. All three drugs had an equivalent suppressive impact on EMG compared to saline while animals treated with succinylcholine showed a more rapid and more complete recovery than animals in the other two drug conditions. Sympathetic stimulation increased HR in all groups and over time baseline HR gradually rose for all groups except the d-tubocurarine chloride animals in whom HR dropped precipitously during blockade and rose gradually during recovery. Systolic blood pressure increased significantly over time but neither of the three drugs differentially influenced the increase. HR deceleration and BP decreases to vagal stimulation were markedly dampened by d-tubocurarine chloride and not by the other two drugs.

The second phase of this experiment investigated the impact of these drugs on aversive respondent conditioning for which a delay-differentiation paradigm was employed. HR accelerative UCRs to shock were largest for the succinylcholine animals, less for the d-tubocurarine

iodide, and quite minimal for the d-tubocurarine chloride groups. Of particular importance to the present investigation is that both succinylcholine and d-tubocurarine chloride prevented a respondent HR differentiation. HR deceleration to the reinforced stimulus was significantly different from the HR response to the nonreinforced stimulus for animals paralyzed by dimethyl d-tubocurarine iodide. However, it is apparent from their data that a trend in the direction of differential conditioning is apparent for the succinylcholine group whereas the interference by the d-tubocurarine chloride infusion is quite profound. Interestingly, however, animals trained under d-tubocurarine chloride who did not manifest differential HR conditioning did so when tested on a second day with dimethyl d-tubocurarine iodide. In general, this study confirmed earlier work demonstrating HR deceleration as the aversive CR and HR acceleration as the aversive UCR for the cat, and illustrated the suppressive effects of HR conditioning by succinylcholine chloride and d-tubocurarine chloride presumably through parasympathetic interference.

Although only these four studies have used cats as subjects, HR deceleration as the CR in the aversive respondent paradigm seems very well established. Furthermore, decelerative CRs are common to cats, rabbits, rats, fish, and lobster. As can be seen in the foregoing, the opposite appears to be true for other laboratory mammals.

PRIMATES. There are several reports of cardiovascular aversive conditioning with primates. (For the purpose of the present investigation, only sub-human primates will be included in the literature review. For a review of cardiovascular conditioning with humans, see Kimmel [1974]). Smith & Stebbins (1965) were the first to report HR acceleration CRs and UCRs and this finding has since been replicated with monkeys (Smith & Nathan 1967; Miller & Caul, 1969; Ferreira, Gollub, & Vane, 1969; Ramsay, 1970; Snapper, Kadden, & Scheonfeld, 1971) and baboons (Ferreira, et.al., 1969). Recently Schneiderman and his students (Schneiderman, Augenstein, & Klose, 1975; Klose, Augenstein, Schneiderman, Manas, Abrams, & Bloom, 1975) also report HR accelerative CRs in the rhesus monkey along with parallel increases in contractility, aortic pressure, and peripheral resistance, with no change in cardiac output. Klose, et.al. (1975) examined the effects of various pharmacologic autonomic blockades on cardiovascular CRs and UCRs. Atropine, a parasympathetic antagonist, raised HR baseline, and in combination with propranolol (a beta-adrenergic antagonist), virtually abolished HR CRs and UCRs. Interestingly, atropine or propranolol alone attenuated but did not abolish these HR responses. High doses of either of these drugs attenuated systolic and diastolic BP CRs which must have been secondary to inotropic and chronotropic effects on the heart since neither directly affects the vasculature.

Ramsay (1970) studied cardiovascular conditioning in the monkey and emphasized the importance of considering pre-CS rates to an adequate analysis and understanding of HR conditioning. He found that HR acceleration was the UCR and CR in the aversive respondent paradigm to replicate most of the work with primates, however, as might be expected, he demonstrated a reciprocal relationship between pre-CS rate and magnitude of the HR CR.

In a similar analysis Snapper, Kadden, & Schoenfeld (1971) employed a pacing technique by stimulation of the S-A node to control pre-CS rate and its effects on CR magnitude. Rhesus monkeys were paced at 150-350 bpm and subjected to 60 trials of a 30-second light CS followed by a 0.3 second 11 m.a. shock. The pacing did not affect the magnitude of the HR CR but did influence the point at which the maximal CR emerged, causing a shift toward the end of the CS as HR pacing rate was increased. Only two animals were employed in the experiment which might suggest that their findings are at this point somewhat preliminary.

In the most recent study with rhesus monkeys, Randall, Brady, & Martin (1975) investigated several cardiovascular dynamics in the course of both aversive and appetitive respondent conditioning. HR acceleration to the aversive CS replicated this very consistent finding for the species. They also found significant increases in blood pressure and dp/dt (rate of change in pressure) for both the left and

right ventricular contractility. They argue that these changes can be accounted for in terms of "sudden increases in sympathetic tone to the SA node and heart musculature, concomitant with the presumed withdrawal... of parasympathetic tone and the appearance of the very precipitate tachycardia (p. 73)". In a similar study published one year earlier, Randall & Smith (1974) investigated cardiovascular components of both exercise and aversive respondent conditioning in the rhesus monkey and found many similarities between the two types of stress. Cardioacceleratory CRs and UCRs were accompanied by increases in left and right ventricular contractility as measured by both the "first derivative" technique and directly by strain gauge. The response to each of the stress circumstances was markedly augmented by propranolol, a beta adrenergic antagonist.

A final study of relevance to cardiovascular conditioning in the monkey was by Pomerleau, Snapper, & Scheonfeld (1969) who demonstrated that conditioned tachycardia is often maintained for as long as 12 hours following the session during which HR is conditioned to an aversive CS and UCS.

Clearly, for infra-human primates, cardioacceleratory CRs are a consistent finding for all studies in which the aversive respondent paradigm is employed. It should be mentioned, however, that at least two investigators have

reported bi-phasic (increase to decrease) HR CRs in some animals (Ramsay, 1970; Sanpper, et.al., 1971). These studies have been interpreted as confirmatory of the acceleratory HR CR for two reasons: First, both studies employed a rather long duration CS (30 seconds) and indicate that the initial increase is followed by a nearly commensurate decrease. With this long an interval, HR must rebound since it is obvious that it cannot increase indefinitely. Second, they report that the second phase decrease does not often reach pre-CS levels by the time the CS is terminated. It would appear legitimate then to consider the entire CS interval an increase at all points over that of the pre-CS baseline.

DOG. The within-species consistency for the cardiovascular components of aversive respondent cardiovascular conditioning with dogs appears to be equally as good as the species reviewed thus far. Earliest reports of aversive conditioning with dogs were from Gantt's laboratory. Dykman, Gantt, & Whitehorn (1956) studied the cardiovascular CR to three different tones each of which was paired with a different intensity of shock. Interestingly, the magnitude of HR increase was not found to increase with shock intensity although precise measures of voltage and amperage are not presented in the report. Also, an adaptation to the shock emerged upon repeated acquisition trials. In a similar study, Dykman & Gantt (1958)

demonstrated dramatic acceleratory HR CRs which, in some animals were completely suppressed by atropine, and in still fewer, only slightly augmented by the administration of atropine. Atropine is a vagal inhibitor which significantly increases baseline HR and consequently affects the potential absolute HR change from pre-stimulus to stimulus intervals.

Another pioneer in studies with dogs is Abraham Black (1965, 1971, 1972) who summarized early work with curarized dogs as demonstrating HR accelerative CRs in some animals, decelerative CRs in others and a biphasic pattern in still others (Black, 1965). Some of his data points to the possibility that HR decelerative CRs are more common to a trace paradigm as opposed to the more frequently employed delay procedure (Black, Carlson, & Solomon, 1962). He also found a reactive influence of the curare preparation which seemed to "'lock' the heart rate at a high level so that very strong stimuli" often could not induce further acceleration. In all of his work, d-tubocurarine chloride was employed as the immobilizing pharmacologic agent and this particular drug is the one with which Howard, et.al. (1975) demonstrated a suppression of basal HR and a profound inhibition of vagally-mediated deceleration during conditioning for the cat. Of particular significance here, however, is that aversively conditioned HR responses for the cat have been consistently deceleratory while, for the dog, acceleratory

HR CRs are the consistent findings for nearly all other investigators but Black. However, in an early study in which dogs were immobilized by a hammock restraint apparatus, Black (Church & Black, 1958) found acceleratory HR CRs in both trace and delay paradigms for both short and long CS-UCS intervals (ISI). In addition, the maximal acceleration emerged significantly later in the long ISI reflecting the Pavlovian principle of inhibition of delay.

In the only other study reflecting between-subject inconsistency, Newton's (1967) brief report indicated deceleratory HR CRs in four dogs and acceleratory HR CRs in three others. Both succinylcholine and d-tubocurarine were used for immobilization and, unfortunately, it is impossible to determine which animals received which drug. Once again, in light of the Howard, et.al. (1975) study reviewed above, this is a critical factor.

In another brief report, Perez-Cruet & Gaertner (1967) found HR acceleratory CRs in no-curarized dogs along with decreases in stroke volume, and increases in right ventricular pressure, thoracic blood pressure, and abdominal blood pressure. Interestingly the decreases in stroke volume generally preceded the acceleration in HR.

In 1966, three studies by Fitzgerald and his colleagues were published in which several procedural variants of aversive respondent conditioning were employed with dogs. Fitzgerald & Walloch (1966) found monophasic HR

acceleratory CRs which were accompanied by increased respiratory amplitudes. Fitzgerald (1966) compared partial (50%) versus continuous (100%) reinforcement and found that acceleratory HR acquisition was marginally better for continuous reinforcement. Moreover continuous reinforcement generated significantly greater resistance to extinction than did partial. However, in a follow-up study, Fitzgerald, Vardaris, & Teyler (1966) demonstrated greater reinforced HR acceleratory CR when extinction was extended by several trials in a second session. Most importantly, all of Fitzgerald's work clearly demonstrated acceleratory HR CRs in dogs which begins to suggest some degree of consistency for the species.

In an interesting study by Pare (1967), two types of immobilization by restraint were studied in dogs. In animals who were relatively free, HR acceleratory CRs were facilitated when compared to relatively restrained animals. Furthermore, the cardiac response to the non-reinforced stimulus in a differentiation paradigm was more rapidly extinguished across trials for "free" versus restrained animals thereby enhancing the rapidity with which the differentiation developed.

Church, Lolordo, Overmier, Solomon, & Turner (1966) investigated HR conditioned and unconditioned responses varying shock intensities with dogs immobilized by tubocurarine chloride. Unconditioned HR acceleration increased

with increasing intensities of shock from 2-8 m.a. and differentially conditioned HR responses were also clearly acceleratory.

Lynch (1968) studied HR in dogs and found acceleratory CRs for nearly all animals but the magnitude of the change was clearly dependent upon pre-CS levels. While there was a fair degree of variability between dogs in early conditioning, the within-subject consistency was quite evident. However, upon repeated conditioning sessions, or overtraining, the between-subject variability gradually decreased as a function of trials.

In a study by Howard, Obrist, Martin, Smithson, & Sutterer (1970), HR and contractility were investigated in four dogs who were subjected to a simple aversive respondent procedure. Acceleratory HR CRs were found which were only slightly augmented by beta-adrenergic blockade. Anticipatory increases in contractility, however, were nearly obliterated by beta-adrenergic blockade.

In one of the few investigations in which a trace paradigm was employed, Antal & Gantt (1970) found significant HR increases to both CS and UCS concomitant with decreases in systemic blood pressure averaging 11-15 mm Hg. Kakigi (1971) found highly significant differences in HR acceleration to a reinforced 1000 Hz tone compared to several non-reinforced tones. Interestingly, initial increases were shown to all tones even in late acquisition,

but the HR increase to the reinforced tone was maintained throughout the duration of the CS while HR return to baseline for the other tones was quite abrupt. Conversely, the initial diastolic BP change to the CS was an insignificant increase while the terminal response was a clear decrease. In addition, HR and BP correlations were quite high during pre-CS and early-CS intervals but fell into an insignificant range during middle to late CS. For the terminal CRs then, HR and BP appear to operate rather independently.

Finally, in a comprehensive investigation, Obrist, Howard, Lawler, Sutterer, Smithson, & Martin (1972) systematically examined HR, contractility, and BP response during aversive respondent conditioning. A simple delay sensitization was attempted. They found dramatic HR increases to both the UCS and the CS for all of their subjects which was minimally but significantly augmented by beta-adrenergic blockade. This finding resolutely confirms the acceleratory nature of the conditioned and unconditioned HR response for aversive respondent conditioning in the dog. In addition to their findings relative to HR, Obrist, et.al., found highly significant increases in contractility which were profoundly altered by beta-adrenergic blockade. They concluded that conditioned HR changes were secondary to the sympathetic effects on contractility. Also, in all animals, significant increases in systolic BP during the CS period

and particularly at UCS offset were found to be attenuated by beta-adrenergic blockade. No reliable changes in diastolic BP were found which further suggested that contractility was of primary significance in the conditioning of total cardiovascular function.

SUMMARY. It appears conclusive that acceleratory HR is the CR common to dogs, primates, and pigeons while deceleratory CRs are peculiar to cats, rabbits, rats, fish, and lobster. It is suggested that, for mammals and birds, this difference might be accounted for on the basis of whether or not "freezing" is a component of the response to aversive conditioning. Freezing has been observed and reported in the laboratory for cats (Bruner, 1969; Hein, 1969) associated with decreased EMG activity (Hein, 1969) and rats (Parrish, 1967; Holdstock & Schwartzbaum, 1965). Rabbits are known to "freeze" in the wild in contrast to the rather obvious "motor startle" more common to dogs, primates and pigeons. Furthermore, it seems possible that the evolution of these characteristic HR CRs developed as species-specific defense reactions (SSDRs) similar to what has been proposed by Bolles (1970) to account for motor avoidance learning. It might be argued that the HR decelerative CRs evolved for animals in whom freezing became an adaptive survival mechanism in the wild (e.g., rabbit) and accelerative HR CRs evolved for animals in whom immediate "flight" to an area of safety acquired adaptive survival

value (e.g., monkey). The characteristic HR pattern therefore come to "anticipate" the consequent "motor state" in response to impending danger. In the laboratory then, remnants of these responses are seen in the fair degree of consistency in directionality of HR CRs for species whose "cousins in the wild" have responded similarly for generations. While this account is admittedly speculative, it is unquestionably testable.

Blood Pressure And Flow

There have been a few studies in which blood pressure and other circulatory measures have been either the only or the primary focus. The earliest systematic examination of vasomotor aversive condition was described by Fromer (1963) in which both operant and respondent conditioning were attempted with rabbits. Blood flow was measured by ear blood volume and a clear respondent CR was established which did not differ significantly from a similar procedure which included an avoidance contingency. Neither the simple respondent nor the respondent plus avoidance contingency differed significantly from yoked avoidance and matched avoidance control groups. However, a simple respondent CR was found in all four of these groups. A complex dual-modality discrimination paradigm was employed for all groups as a control for sensitization and the complexity of the task might well have interfered with the development of an operant CR. Fromer's data presentation

is lacking in two respects: 1) Had he presented latency measures, evidence for operant learning could be more readily evaluated, and 2) There is no indication from his data relative to the directionality of the blood volume CR. Instead, a "mean per-cent discriminated CR" was employed for all analyses which obscured the precise nature of the conditioned vasomotor response. Also, contemporary references to Fromer's study reflect curious inconsistencies. For example, Snyder & Noble (1968) submit that Fromer failed to find strong evidence of vasomotor operant conditioning; Hamano & Okita (1972) refer to the study as the first demonstration of autonomic operant conditioning; and Black (1969), in the same paper, cites Fromer as among those investigators demonstrating successful operant autonomic conditioning (p.25) while later pointing out that he failed to demonstrate operant conditioning of vasomotor responses (p.28-29). It is clear from the original report that Fromer did not demonstrate operant vasomotor conditioning at all. He did, however, find conclusive evidence of a respondent vasomotor change.

Smith & Stebbins (1965) investigated blood flow respondent conditioning using an ultrasonic flow probe on the terminal aorta of six monkeys. In the context of a discriminative aversive procedure, they demonstrated quite dramatic increases in both aortic flow and heart rate to the shock UCS and CS+ which were claimed to be independent of

either respiratory or skeletal muscle activity. Importantly, they also found that conditioned blood flow latencies were highly uniform from trial to trial.

Studies of conditioned blood pressure seem to differ often by virtue of the locus of measurement. For example, the Smith & Stebbins study demonstrated flow increases at the terminal aorta which would suggest decreased pressure at that location in spite of the fact that relevant data were not presented. Perez-Cruet & Gaertner (1967), on the other hand, reported increases in pressure during the CS but the measurement was at the site of the thoracic and abdominal aorta, or much more peripherally than Smith & Stebbins. Antal & Gantt (1970) described conditioned blood pressure decreases at the carotid artery concomitant with blood flow increases in the femoral artery perfusing the leg to which shock was administered in a leg flexion study. Ferreira, Gollub, & Vane (1969) in an almost identical procedure showed systolic and diastolic CS increases at the carotid although there was no leg-flexion conditioning employed and monkeys were used as subjects rather than dogs. Schneiderman, Vandercar, Yehle, Manning, Golden, & Schneiderman (1969) also found carotid blood pressure increases to a CS and UCS in rabbits which was demonstrated to compound a HR decrease CR presumably via the baroreceptor feedback loop. Kato, Gozsy, & Lemieux (1970) in a complex technical report demonstrated intricate

microcirculatory changes to an aversive CS and implicated a change in balance between dilator bioamines (histamine and serotonin) and the constrictor catecholamines (dopamine and norepinephrine) which served to mediate the vascular response. The response they measured was vascular tonus in the skin of rats and the CS and UCS were a visual stimulus and a 50 ma ECT respectively. Actually this is not a usual aversive respondent paradigm since ECT obviously affects consciousness during its administration and is known to have a profound impact on "recent memory". In any event, it is worth noting that Kato, et.al., found increased peripheral resistance to the CS suggesting marked peripheral vasoconstriction.

In a study of particular relevance to the present investigation Bergamaschi, Caravaggi, Mandelli, and Shanks (1973a) demonstrated significant increases in left circumflex coronary flow as a UCR to the firing of a gun. Concomitant increases in HR, cardiac output, and left ventricular work with decreases in peripheral and coronary resistances were also found. Interestingly, no significant changes in aortic pressure were reported. When the gun firing was preceded by a tone, rapid acquisition of anticipatory increases in coronary flow was found to occur with HR deceleration and central aortic blood pressure increases (Bergamaschi, Caravaggi, Mandelli, & Shanks, 1973b). Presumably the baroreceptor system would again seem

responsible for this latter finding. These effects were augmented by sympathetic beta-adrenergic blockade. It should be mentioned that only three dogs were used in the study and they were not immobilized by neuromuscular blocking agents.

A final study related to the present investigation which merits consideration is an anecdotal report by Newton & Ehrlich (1969) who noted coronary vasodilation in dogs who were exposed to a sudden entrance of people into an experimental room in which the animals had been treated. They were unable to determine specifically whether the response was an unconditioned "effect of person" or whether the person acquired properties of a potential UCS by occluding the animals' coronary artery subsequent to each entrance of the room.

These latter studies strongly suggest that the coronary system is highly responsive to environmental events and may well be modifiable by several conditioning procedures. The present investigation seeks to examine systematically the potential for learned control of coronary circulation in the context of the respondent aversive paradigm with dogs immobilized by a neuro muscular blocking agent. Attention will also be directed to several other cardiovascular functions to more precisely determine the interrelationships between the measures and to compare these findings to previous research.

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FOOTNOTES

1. The brief review of cardiovascular function owes a great deal to the work of Attinger (1971) and Wiggers (1957).
2. The review of coronary circulation is a synthesis of selected material from Gorlin (1971, 1974) and Feigl (1972).
3. The chart illustrating factors which influence coronary flow is a synthesis of selected material from Gorlin (1971, 1974) and Feigl (1972).