

**CARDIAC FITNESS SIGNS AFTER  
STRESS-FREE RUNNING WHEEL  
EXERCISE IN RATS**

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ABSTRACT

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CARDIAC FITNESS SIGNS AFTER

STRESS-FREE RUNNING WHEEL

EXERCISE IN RATS

Rats were trained in a food rewarded running program rather than the usually implemented type where punishment is used to motivate running. Trained rats were first assessed for cardiovascular fitness as a result of this type of training, and then, their responses to the psychological stress of an open-field test was compared with those of non-exercised control groups. Runners were given peanut butter reward for increasing their day-to-day running wheel exercise during the 10 week program. From the middle to the end of the program, heart rate was monitored weekly. At the end of the program Runners and the two control groups were tested for emergence latency, squares crossed, urination and defecation in an open-field. Heart rate (EKG) response increased equally for all groups after the stress of handling during the EKG procedure or because of food or food expectancy during the running period. Runners recovered faster than other groups from this stress. Runners decreased emergence time in the open-field over sessions while other groups did not. The psychological stress due to handling, reward expectancy or reward, was unexpected. Chronic exposure to the stress of Exercise reduced the response to psychological stress either by making Runners less sensitive in their peak heart rate response

to this stress, or by making them capable of more rapid heart rate recovery. Runners habituated more quickly to the stress of the open-field, as reflected by emergence times. Very rapid emergence times suggest that a more stressing open-field condition should be used in future studies. Data from the present study suggest that if reliable fitness could be established with refinement of this paradigm it might be a better analogue of human fitness effects than other available analogues due to its absence of punishment used to motivate animals to run.

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## Table of Contents

	Page	
Introduction	1	
Section I	Definitions of Stress	2
Section II	Notions of Cross-Tolerance And Cross-Resistance	3
Section III	General Versus Specific Stress Responses	4
Section IV	Stressful Stimuli	7
Section V	Stress Responses	10
Section VI	Tolerance and Cross-Tolerance	12
Methods	28	
Results	38	
Discussion	61	
Footnotes	67	
References	68	

This investigation examines the concept of stress as well as ways an organism has of coping with different stressors. The specific question addressed in the study described below is, whether exposure to a physical stressor, running, changes an animal's response to a psychological stressor, exposure to an open-field. There are many problems in the literature related to definitions of stress and stress responses, as well as the arbitrary distinction frequently made between physical and emotional stressors and stress responses. The notions of tolerance and cross-tolerance, borrowed from pharmacology, offer potential models for understanding the mechanisms by which an organism develops resistance to stress. Chronic exposure to a stressor such as exercise can produce either a tolerance to that particular stressor, or, it may produce a cross-tolerance to other stressors. This developed tolerance or cross-tolerance would help minimize the ensuing wear and tear on the body. This section attempts to clarify the confusion in the literature related to the concept of stress and stress responses and describes how the various bodily systems function together to help the organism better tolerate stress.

SECTION I

DEFINITIONS OF STRESS

Semantic Confusion

There is often semantic confusion in discussions of stress since some investigators treat stress as an environmental stimulus and others treat it as the organism's response to that stimulus. Dictionaries provide technical and non-technical examples of each type of definition:

In technical definitions, a clear distinction is made between the terms "stress" and "strain". In Webster's Unabridged Collegiate Dictionary "stress" is defined as the force exerted upon a body while "strain" is defined as the body's response to that force.

When non-technical definitions are used, confusion arises because the two terms, stress and strain, are used interchangeably. Stress is in some cases treated as the force being exerted while it is in other cases treated as the response to such a force. Webster provides both types of definitions and doubly confuses the issue by including each of these terms within one given definition. For example, "a condition existing within elastic material because of strain or deformation by external forces". Random House Dictionary separates its definitions into two categories, "mechanical" and "physiological", but again "stress" and "strain" are used interchangeably. Selye (1976) states his linguistic inability to distinguish between the term "stress" and "strain" as having been the historic source of the

confusion.

### Ways To Minimize The Confusion

To eliminate confusion in the present study, "stress" will be used to describe the force or condition exerted on the body, while "stress response" will be used to describe the body's reaction to such stresses. Furthermore, each of these terms will be operationally specified when they are used. Thus in a particular section running wheel exercise, for example, may be specified as the "stress" and increased heart rate, for example, may be defined as the "stress response".

## SECTION II NOTIONS OF CROSS-TOLERANCE AND CROSS-RESISTANCE

Tolerance and cross-tolerance are terms borrowed from pharmacology. Drug tolerance has been defined as the process by which drug sensitivity is reduced as a function of drug experience. Cross-tolerance is defined as a decreased sensitivity to one drug which results from experience with another drug. When two drugs show cross-tolerance, it is presumed that the two drugs have actions on a common mechanism.

Sensitivity to stress, like sensitivity to drugs, decreases as a function of some kinds of experience. For example Selye (1976), has noted that adrenocortical activity rises sharply during the beginning of a stressful event, then tapers off to a level slightly above normal, if the stressful event continues. This tapering off of adrenocortical activity occurs during Selye's "resistance" phase, and therefore is not due to



exhaustion or an inability of the cortex to maintain high levels of activity. Sensitivity to one stressor can decrease as a function of experience with another stressor. Thus the concepts of tolerance and cross-tolerance could be applied to stress, and cross-tolerance between stressors could be inferred to involve a common stress mechanism for the two stress stimuli. Such a concept is reflected in Selye's discussions of "specific resistance" and "cross resistance" where resistance is used in the same sense as tolerance. Selye assumed a common stress mechanism when he found that there was cross-resistance to one stressor developed as a function of experience with another stressor.

Drugs and stressors can be given acutely, where only one exposure is provided, or where sufficient time between exposures is allowed to preclude the development of resistance, or chronically, where exposure is given often enough to cause development of resistance. Tests of cross-resistance would typically involve chronic exposure to one stress stimulus, and acute testing of the response to a second stress stimulus. Cross-resistance between the two would imply a common stress response to the two stimuli.

### SECTION III GENERAL VERSUS SPECIFIC STRESS RESPONSES

#### Introduction

Though stress responses have been arbitrarily categorized as being either general or specific in nature, in actuality these responses include components of both. A

general stress response is conceived as a multifaceted response elicited by all stressors and producing cross-tolerance between them. A specific stress response, on the other hand, would be unique in character, elicited by its own specific stressful stimulus where tolerance would develop only to that specific stimulus. However, as it exists in nature, the stress response has both general and specific qualities. Some stressful stimuli are more able than others to prime the system for adapting to or resisting other stressors. Ostman & Sjostrand (1975), found that the stress of running was better able to prime the system for resisting other stressors than the stress of a cold environment.

#### Selye's Concept

Selye (1976), describes the overall response to a stressor as consisting of both specific and non-specific components. That is, any stressor which acts upon an organism produces both specific and non-specific effects. Though Selye has coined the term "GAS" or General Adaptation Syndrome to describe the non-specific part of the response, he has not coined an equivalent term for the specific part. Here it will be referred to as the "SAR" or Specific Adaptation Response. The GAS is that part which is always elicited no matter which stressor is doing the eliciting. Selye has noted three types of changes which occur together consistently in response to any stressor: the adrenal cortex hypertrophies and increases its activity; the thymus, spleen, lymph nodes and all other lymphatic tissues atrophy; and the stomach and duodenum develop ulcerations. These changes

occur to different degrees depending on the strength of the stressing agent. The specific part of the response, the SAR, is that part which is unique in character, elicited by its own specific stressor. Examples of specific responses might be the organism's increased rate of breathing in response to lack of oxygen, or a highly specialized adjustment such as strengthening of specific muscle groups in response to chronic usage. Selye emphasizes that all stressors elicit a general as well as a specific response and it is the specific part of the response which must be removed in order to uncover or isolate the GAS. The GAS is the lowest common denominator of all stress responses for Selye, and it is on this syndrome that he chooses to focus his interest.

#### Alternate View Of The Stress Concept

Mason (1971) discusses new findings that have emerged in studies of endocrine regulation which have important implications concerning "stress" theory. He questions Selye's concept of a general syndrome showing that at least some stressors can cause different responses from others in the pituitary adrenal cortical system. For example, Mason has demonstrated that when cold is used as a physical stressor urinary hydrocorticosterone (the metabolic byproduct of adrenal cortex activity) increases, whereas when heat is used, urinary hydrocorticosterone decreases. Exercise or fasting, on the other hand, cause little change in these levels. Thus, the adrenal cortex does not always increase its activity in response to noxious stimuli. Mason

went on to suggest why Selye might have thought such a general syndrome was prevalent. Researchers studying the endocrine response to physical stressors, such as heat, cold, exercise or fasting, have come to realize that the endocrine system is extremely sensitive to psychological factors which went uncontrolled in Selye's work. Thus, the situation was more complex than Selye realized due to the difficulty of separating the effects of the stress stimuli in his experiments from a variety of psychological factors such as frustration, fear, discomfort, novelty or threat, all of which may have accompanied the testing situation, but only some of which were factors addressed within his experimental paradigms. To the degree that Selye failed to appreciate common factors in different paradigms, he would have confused general responses to the test situation with the more specific responses to test stimuli. Some examples of uncontrolled contributing factors might be handling (Levine, 1960), novelty (Levine, 1971), and daylight (Rusak & Zucker, 1975).

#### SECTION IV STRESSFUL STIMULI

##### Physical Stressors

There are wide varieties of both physical and psychological stressors utilized by investigators of stress. Physical stressors can be administered to an organism either

via the external or internal environment. Investigators like Berger et al (1980), Levine (1960), Denenberg (1963), McCarty (1979), Anisman & Sklar (1979), Williams and Eichelman (1971), Miller et al (1978), and Miller and Maloy (1977) have used shock as a physical stressor. Levine (1960), Kramar (1953), Bartlett (1956), Zimkin (1964), Katz (1979) and Ostman-Smith (1979) described the effects of exposure to cold, where as Zimkin (1964) and Mason (1971) described those due to exposure to heat. Engle (1953) used illness while Levine (1960) and Zimkin (1964) discuss the uses of leukemic cells, toxic levels of glucose, or other toxic chemicals as physical stressors. Thus, investigators of stress have used a wide variety of physical stressors either introducing them into the body of the organism or into the external environment surrounding it.

#### Psychological Stressors

Psychological stressors are stimuli or situations in the external environment which are stressful, not because they are painful or noxious, but, it is assumed, because they are unpredictable, uncontrollable, or perceived as threatening in some way (Weiss, 1968; 1970). These stressors are not listed among physiological stressors primarily because of the difficulty investigators have in specifying them by their physical properties. Psychological stressors are, in fact, physiological stimuli, but their physical dimensions are often poorer predictors of their stressfulness than are their conditioned associations or

presumed (unconditioned) significance for the subject. Investigators such as Brady (1958) and Weiss (1968, 1970, 1979) have given different groups of animals equal intensities, durations, and frequencies of electric shock yet some groups have consistently developed more severe gastrointestinal lesions than others. It must therefore be assumed that less obvious variables, other than intensity, duration and frequency of shock, were critical components of the stressful event. Both Brady and Weiss have tried to isolate the elusive components though the two had different ideas as to what they might be. Brady has discussed such factors as the demanding condition of having to press a lever to avoid shock as well as the "social" interaction between "executive" and yoked control animals, where one has the responsibility of avoiding shock for both, as important contributors to ulcer severity. Weiss, in interpreting very similar experiments, suggested that the ability to control the shock decreased rather than increased the stress of the situation. That Brady and Weiss can agree as to the dimensions of the physical stressor (shock intensity, duration, and frequency) but not about the dimensions of the psychological stressor, illustrates the fact that the psychological category reflects the more poorly understood and least definable components. Other investigators have looked at such things as handling, physical restraint, tunnel emersion time, bright light, novel environment and different rearing conditions in their attempts to assess the role of psychological factors in stress. For example,

Levine (1960), Denenberg (1963), Denenberg & Smith (1963), Denenberg & Grota (1964) and Weininger (1954) have studied handling as a psychological stressor. Bartlett (1956) and Weininger (1954) have studied physical restraint. Tharp and Carson (1975) have studied tunnel emersion. Bartlett (1956) studied bright light while Levine (1971), Studelska & Kemble (1979) and Denenberg & Grota (1964) have studied other novel environments besides those mentioned above. Whimbley and Denenberg (1967), Denenberg & Grota and Holloway, Dollinger & Denenberg (1979), investigated different rearing conditions as psychological stressors. These and other physical and psychological stressors are used by investigators as tools to observe how different organisms respond to, or cope with, unpredictable, uncontrollable, or otherwise threatening conditions in their environment. Though psychological stressors are more elusive than physiological stressors due to the difficulty investigators have in specifying them by their physical properties, they are still useful in research since they can represent stressful life events.

## SECTION V            STRESS RESPONSES

There are wide varieties of both "physiological" and

"emotional" responses studied by investigators in the field of stress. The distinction made between physiological and emotional responses commonly used in the literature is a false one, since, in actuality these responses are not mutually exclusive. It is in the area of emotional responses that this false distinction between emotional and physical becomes a problem, since emotional responses are presumably reflections of physiological activity. This is further demonstrated by the operational definitions of emotion which involve autonomic responses, such as changes in heart rate and hormonal levels. Thus it is difficult to discuss emotional responses as being distinct from physiological ones. Recognizing this difficulty, stress responses will be presented in this section according to whether the stressors which elicited them were considered physical or psychological in nature.

#### Responding Associated With Physical Stressors

A variety of physical stressors have been used in the laboratory situation as a means of observing an organism's responses to stress. The responses measured have been just as varied. Neuroendocrine responses such as adrenocorticotropin hormone (ACTH), steroids produced by the adrenal cortex, norepinephrine (NE), and epinephrine (E), were measured by Levine (1960), Engel (1953), Kramar (1953), McCarty (1979), Anisman (1979), Berger et al (1980) and Ostman and Sjostrand (1975) in response to such physical stressors as shock, cold, leukemic cells and toxic agents. Levine (1957; 1960) and Zimkin (1964) noted survival time after administration of pathogenic agents. Levine (1960) measured body weight and gastric intestinal ulcers,



while Miller, Grossman, Richardson, Wistow & Thomas (1978) and Miller & Malov (1977) noted cardiac damage as a result of shock. Katz (1979) measured endorphins following cold water emersion. Engel (1953) recorded the glucose/insulin response to illness and Kramar (1953) noted capillary resistance to cold. Berger et al (1980) measured plasma cholesterol changes following shock, and Williams & Eichelman (1971) recorded tail blood pressure changes as a result of shock.

#### Responding Associated With Psychological Stressors

A variety of psychological stressors have been used in the laboratory, as the physical stressors were, also as a means of observing the organism's response to stress. Levine (1971) and Engel (1953) measured the neuroendocrine responses (ACTH, corticosterone, NE, E, and adrenal weight) to such psychological stressors as withholding of an appetitive reinforcement. Levine (1960) measured rate of growth after handling and Weininger (1954) looked at gastro-intestinal ulcers and heart damage following handling. Bartlett (1956) and Weininger (1954) both measured body temperature in response to the psychological stressors, restraint and handling.

#### SECTION VI TOLERANCE AND CROSS-TOLERANCE

The phenomena of tolerance and cross-tolerance offer potential models for understanding stress related disorders. Both psychosomatic and various emotional disorders are included

within this category. Physiological manifestations thought to be associated with some underlying stress are often part of the presenting symptomatology. Because these manifestations can be disabling, if not life threatening, methods for developing resistance to stress are of interest.

### Psychosomatic Disorders

Psychosomatic disorders are those resulting from the influence of emotional stress or conflict on a predisposed somatic organ or system. In these conditions there is a recognized physical disease or disorder brought on by or exacerbated by some emotional factor. Illness such as peptic ulcer disease, hypertension, neurodermatitis, colitis, migraine headaches, hyperthyroidism, atherosclerosis and asthma, are often spoken of as having psychosomatic determinants but many other diseases have been considered as well. Selye lists a variety of symptoms as being indexes of stress. Many of these such as pounding of the heart, diarrhea, vomiting, and migraine headaches, are also symptoms of psychosomatic disorders. One assumption about psychosomatic disease is that different individuals have different organ sensitivities and thus different individuals display different organ symptoms in response to any stressor that activates the GAS.

### Emotional Disorders

Emotional disorders or psychoneuroses are generally viewed as maladaptive attempts to deal with fear or anxiety. They include phobias, obsessive compulsive neuroses, hysterical neuroses, and anxiety and depressive reactions,

all of which are thought to be exacerbated by stress, particularly by stress related to the anxiety or fear in question. Included in Selye's list of indexes of stress, some of which have been mentioned in relation to psychosomatic disorders, are a number of symptoms which are related to psychoneuroses such as insomnia (often an indicator of emotional tension), inability to concentrate, pounding of the heart, general irritability, sweating, hyperexcitation, or depression. Most of these symptoms seem to be related to a state of general arousal, a priming of the organism's bodily systems for action, whereas those symptoms usually associated with psychosomatic disorders are more organ-specific. In the case of the symptoms associated with psychoneuroses, it seems that different individuals display similar general arousal states in response to a variety of different stressors. Whether these stress related symptoms are expressed as a state of general arousal or are more organ specific in nature, their disabling effects may be avoided or minimized by using treatment methods modeled on the phenomena of tolerance and cross-tolerance.

#### Tolerance: A Method For Developing Resistance To Stress

Exercise, systematic desensitization, and flooding, all represent methods for developing resistance to physiological and emotional stress by developing tolerance to the stressor.

#### Exercise

Exercise is a technique which utilizes repeated exposure to

a physical stressor (such as oxygen debt) as a means of decreasing the stress response elicited by that stressor.

#### Types of exercise

Exercise can be carried out in a variety of ways ranging from short intense sessions to more prolonged less intense ones. Some types of exercise, such as weight lifting and sprinting, tend to develop power or strength, while other types, such as long distance swimming or jogging (running), have a tendency to develop endurance. Different schedules of exercise, such as single or intermittent exposures (acute), demonstrate the subject's baseline state of fitness, while chronic exposure to physical exertion produces adaptation which causes relatively long term changes in some components of fitness.

#### Tolerance effects of exercise

The type of exercise program chosen will affect how the body adapts itself to that particular stressor. Some programs seem to allow the organism to develop the ability to tolerate a greater variety of stressors than other programs. Adaptive mechanisms due to chronic exposure to exercise<sup>13</sup> (running) occur in the neuroendocrine system, skeletal muscles, cardiorespiratory and metabolic systems which work together, making the body more efficient in providing fuel and oxygen for the working muscles (Fox, 1979; Edington & Edgerton, 1976; Guyton, 1976). The neuroendocrine system affects the body by direct neural stimulation as well as by hormones secreted into the bloodstream. Often there is overlap between neural and hormonal activity so that organs receive dual stimulation. With exposure to chronic

exercise, the autonomic nervous system steps up its activity thus aiding the other systems of the body to build up a tolerance to the increased demands put upon them. Some information on the general functioning of the neuroendocrine system will demonstrate how this complicated communication system coordinates the other systems while under the stress of exercise.

During exercise the sympathetic nervous system increases the rate and force of the heart beat directly and stimulates the adrenal medulla to secrete norepinephrine and epinephrine into the blood (Guyton; 1976). The increased demand on the adrenals due to exercise or emotional stress causes them to hypertrophy. Norepinephrine and epinephrine usually work as a team when stimulating the various parts of the body, one acting as a stimulator and the other an inhibitor to produce, through their degree of imbalance, the required degree of activity. Epinephrine is more effective in increasing cardiac output and metabolic rate (increased rate of glycogenesis in the liver and muscles; increased rate of glucose released into the blood) while norepinephrine is more effective in increasing the total peripheral resistance to avoid vascular shock. The cardiovascular system seems to develop an increased sensitivity to norepinephrine due to repeated exposure to the stress of exercise (Ostman-Smith, 1979). This would seem to allow the cardiovascular system to meet changing demands more quickly and with less prompting. The parasympathetic nervous system has the opposite effect from the sympathetic nervous system on various organs such as the heart muscle, coronary arteries, bronchi and

intestines (Guyton, 1976). For example, it decreases the rate and force of the heart beat directly by its action on the Vagus nerve, constricts coronary arteries, mildly constricts the bronchi and increases peristalsis. Because of these effects the parasympathetic nervous system would not seem to play an important role during exercise but would take over once exercise was terminated to help bring the various bodily systems back to baseline levels of functioning. Maybe it is for this reason that changes due to repeated exposure to exercise have not been studied.

Cortisol, a hormone released from the adrenal cortex, has the same effect on metabolism as epinephrine, increasing the production of glucose in the liver and inhibiting glucose uptake and oxidation by many parts of the body. Like norepinephrine, cortisol enhances vascular activity to avoid vascular shock and actually allows norepinephrine to induce vasoconstriction. The nervous system works together with the hormones to co-ordinate the bodily systems in developing a greater tolerance to the stress resulting from chronic exercise (Guyton, 1976).

The skeletal muscles are a system which develops tolerance to the stresses of exercise by increasing their ability to exchange gasses (oxygen and carbon dioxide) as well as increasing their efficiency in the utilization of fuels. These changes due to chronic exposure to exercise are directly related to the types of exercise used (eg. strength vs endurance training) (Fox, 1979). In strength training the emphasis is on a change in contractile mechanisms. The muscles hypertrophy causing their mitochondria to increase in both size and number, thus supplying

more cells to deal with the increased work. This improves the muscles' ability to supply high energy phosphate--adenosine triphosphate (ATP)--necessary for the production of work. In endurance training the emphasis is on a change in metabolic mechanisms. The concentration of about 20 enzymes is increased as is their rate of activity, allowing for the increased metabolism of glycogen, a fuel necessary for the resynthesis of ATP (Edington & Edgerton, 1976). The muscles develop the ability to store more glycogen as well; thus allowing for an increased store of readily available fuels. They become capable of metabolizing increased amounts of fats relative to carbohydrates making them more versatile in their usage of fuels and allowing them to accumulate less lactic acid. There is an increase in capillary development providing a larger surface area for the exchange of gases thus increasing the efficiency for extracting oxygen from the blood (Fox, 1979). There is also an increase in myoglobin in the muscle cells which provides a source of oxygen when the usual supply is depleted due to the increased demands of exercise. The muscle tissues adapt in such a way as to be maximally efficient in transporting and utilizing both oxygen and fuels to keep the muscles functioning under prolonged exertion. This increased ability to adapt to prolonged physical exertion means the body is better able to tolerate such a strain.

The cardiorespiratory system provides for the uptake and transport of oxygen to the working muscles as well as for the removal of wastes such as carbon dioxide and lactic acid. This system adapts in a variety of ways to better deal with the

increased demands for oxygen and the increased need for waste removal. With chronic exposure to exercise the heart hypertrophies, increasing its general strength and its force of contraction (Guyton, 1976; Fox, 1979). If endurance training has been used, the volume capacity of the ventricles increase while the thickness of the heart muscle remains relatively constant. This combination of larger ventricular cavities and stronger ventricular contractions is associated with an increase in stroke volume. The resting heart rate becomes lower and greater work intensity can be performed at a given heart rate. The heart muscle also becomes more resistant to hypoxia (low oxygen) due to the increased number of mitochondria and the ability to use lactate as fuel when the availability of oxygen is diminished. Finally, the blood volume increases as does the hemoglobin concentration, allowing more oxygen to be transported to the muscles for each contraction of the heart. All of these changes make the heart more efficient in pumping the blood, and allow it to continue functioning adequately even when its own oxygen supply has been diminished, due to the stress of prolonged physical exertion.

With chronic exposure to exercise the lungs also adapt to the increased demands put upon them by increasing their volume, thus making more oxygen available to the cardiovascular system (Fox, 1979; Guyton, 1976). To further improve the efficiency of oxygen transport to the muscles, the capillaries develop the ability to extract more oxygen from a given volume of air. If these adaptive mechanisms are unable to meet the oxygen needs of the working muscles, the lungs increase their rate of



ventilation, thus providing a more rapid turnover of fresh air for the oxygen transport system.

The metabolic system provides the body with the energy it needs during exercise receiving input from the neuroendocrine system and skeletal muscles. Fuels can be metabolized either aerobically or anaerobically (Guyton, 1976). With aerobic metabolism carbohydrates and fats are efficiently broken down with the help of oxygen to produce the energy necessary to fuel biological processes without the formation of lactic acid. With anaerobic metabolism, however, carbohydrates are inefficiently broken down, due to the absence of oxygen causing the byproduct lactic acid to be produced. If the body cannot utilize or get rid of the accumulating lactic acid from the working muscles, these muscles' ability to function will be hampered. Despite the disadvantage of lactic acid build up, the anaerobic system provides a quick but short lived source of energy necessary for the biological processes occurring during short but strenuous periods of exercise (Guyton, 1976). Endurance training tends to develop aerobic relative to anaerobic metabolism (Fox, 1979).

Thus chronic exposure to the physical stresses of exercise develops adaptive mechanisms in the different bodily systems which help the organism to tolerate, more effectively, the extra demands placed upon it during such exercise. In other words, exercise leads to the development of stress tolerance in many systems of the body.

#### Systematic Desensitization and Flooding

Systematic desensitization and flooding are also

techniques which utilize repeated exposure to a stressor as a means of decreasing or eliminating the response elicited by that stressor. Systematic desensitization uses multiple and gradually increasing intensities of exposure to an anxiety provoking situation to reduce the response to that situation. Flooding, on the other hand, uses multiple exposures to an anxiety provoking situation, but instead of gradually increasing the intensity of the situation, so as to avoid overloading the client, uses the most intense condition right from the onset of therapy. The high arousal elicited by this "sink or swim" approach is expected to expose the underlying causes of fear so that they may be confronted, thereby reducing the anxiety response. Whether the emotional stressor is presented in large doses or small ones, each procedure involves the repeated exposure to that stressor.

#### Cross-tolerance: A Method For Developing Resistance To Stress

Another potential method for developing resistance to stress would exploit the phenomena of cross-tolerance. An organism chronically exposed to one stressor might develop adaptive mechanisms effective in dealing with other stressors.

#### Cross-tolerance Between Two Physical Stressors

If an organism is chronically exposed to a physical stressor, the adaptive mechanisms developed as a result of this repeated exposure may carry over to other physically stressful situations. Different stressors have been used to demonstrate

this.

#### Cross-tolerance between shock and other physical stressors

Many of the adaptive mechanisms developed through exposure to chronic shock are effective when the organism has to later deal with other physical stressors. Levine (1960) found that rats previously exposed to repeated bouts of mild shock in infancy, showed less reactivity as adults to physical stressors such as toxic injections of glucose and swimming in a water maze. This previous exposure to the stress of mild shock resulted in the animals developing a cross-tolerance to a different stressor such as the toxic agent glucose, where it was demonstrated that these animals survived longer. When circulating steroids were measured immediately following the current bout of electric shock, it was found that the animals which had had previous chronic exposure to the stress of mild shock in infancy showed a much higher output of adrenal steroids, such as corticosterone, in the first 15 minutes after the presently administered shock, whereas before this shock both groups' levels of steroids were equal. The rats which had not been previously exposed to chronic stress in infancy achieved the same output of steroids after shock but these levels were reached more slowly and remained elevated longer than those of the groups previously exposed to stress. The greater speed and shorter duration of the steroid response in those animals previously exposed to chronic stress might improve their ability to tolerate new stressors by having their

defense mechanisms already primed for quick efficient action and by allowing these mechanisms to stop functioning as quickly as possible once they are no longer needed (Levine, 1960).

#### Cross-tolerance between exercise and other physical stressors

Many of the adaptive mechanisms developed through one particular type of chronic physical exercise, such as jogging, are also effective when the body has to deal with other types of exercise such as the bicycle ergometer or swimming, or with other physical stressors such as cold, heat and toxic agents. The body has to make less of an effort in adapting to these new stressors, thus increased tolerance for these stressors is demonstrated. Ostman-Smith (1979) has compared rats who have undergone chronic exposure to swimming with those that received chronic exposure to cold and found that both groups showed the same degree of cardiac and adrenal hypertrophy. The cardiac and adrenal hypertrophy are signs of adaptation developed in the cardiac and hormonal systems as a result of the increased stress of either cold acclimation or swimming training and these reflect tolerance effects. Because of the same degrees of hypertrophy one might assume that chronic swimming and chronic exposure to cold were equally stressful in this experiment. When exercised and cold acclimated rats were put in a novel environment (at normal room temperature) both groups excreted less norepinephrine than controls, suggesting that both swimmers and cold acclimated animals were more easily able to adapt to the novel environment than were the controls

since these groups secreted less norepinephrine. During subsequent cold exposure, both exercised and cold acclimated groups had less of an increase in norepinephrine secretion than did the controls. This demonstrates development of tolerance to cold stress in the one group and cross-tolerance between exercise stress and cold stress in the other.

In another example Zimkin (1964) looked at cross-tolerance developing between physical training and such things as cold stress, heat stress, and administration of toxic substances (such as trichlorethylamine and X-irradiation), and the stress associated with transplanted malignant tumours. For cold stress he measured time lapse before onset of convulsions, while for toxic substances and heat stress he measured survival time. He also found that moderate exercise is more effective than excessive exercise in producing this cross-tolerance while too little exercise is ineffective.

#### Cross-tolerance Between The Physical Stressor, Exercise, And Psychological Stressors

If an organism is chronically exposed to the physical stressor, exercise, the adaptive responses it develops as a result of this repeated exposure may carry over to psychologically stressful situations. The adaptive effects of chronic exposure to exercise on the bodily systems have already been described. Some of the adaptive mechanisms may also be effective when the body must deal with psychological stressors such as restraint or the open-field.

### Previous studies

Previous studies have shown that adaptation to a physical stressor allows animals to improve their ability to tolerate novel psychological stressors. Bartlett (1956) attempted to see if cross-tolerance would develop between the physical stressors cold or exercise and the psychological stressor restraint. The organism's response to restraint was measured by the hypothermia which developed from that immobilization. Rats were first run to exhaustion for 12 consecutive days and then exposed to cold and restraint simultaneously. This combination of running followed by cold and restraint produced some inhibition of hypothermia (cross-tolerance) though this did not occur in animals that had had exposure to running for only six days. Adaptation to a seemingly unrelated stressor, forced running, may protect against the threatening situation of restraint.

Tharp and Carson (1975) also assessed whether cross-tolerance would develop between a physical and a psychological stressor. They first exposed rats to an eight week program of the physical stress of either running or swimming and then to the psychological stress of a novel situation, the open-field. Runners and Swimmers each performed differently in the open-field from the controls. Runners and Swimmers entered significantly more total number of squares than did the controls. The control groups defecated significantly more and had longer latencies in leaving the first square. Thus cross-tolerance developed, to some degree, between the physical stressor, exercise, and the psychological stressor, the open-field. These and other investigators of the effects of running have usually confounded

running with other stressors, such as shock or a motorized running wheel (where the animal gets "tumbled" about in the wheel if he slows down or stops running. These are used to force the animals to run. Thus, from these studies, it cannot be determined whether the observed cross-tolerance was between running and the subsequent psychological stressor, or rather between the associated stress of shock or the moving treadmill and the psychological stressor.

#### The present study

The present study was designed to determine whether chronic exposure to the physical stressor, running, could produce cross-tolerance to the stress of the novel situation, the open-field. Three groups of animals were utilized, Runners and two different control groups, Matched Controls and Caged Controls. Matched Controls were employed to account for the effects of the extra handling as well as those of the running environment. Caged Controls were employed to demonstrate how animals might respond not having received the extra handling or the experience of running in that particular environment.

Runners performed daily in the activity wheels. Unlike the study by Tharp and Carson, this group was food-rewarded for running without the additional use of such threatening conditions as shock or a motorized activity apparatus as a stimulus to foster running. This would allow for adaptation or tolerance to develop to the increased work load of the chronic exercise alone, rather than some combination of that work load plus the added stress due to shock or the forced activity caused by the

motorized equipment. Matched Controls received the identical treatment as Runners except their activity wheels were stationary. Caged Controls remained in the home cage during this treatment.

Heart rates were measured weekly for all groups. At the termination of the exercise program, Runners' and non-runners' behavior scores were compared in the novel environment of the open-field.

It was expected that tolerance to the stress of exercise would develop using a food rewarded running program and would be reflected in either decreased heart rate response to, or increased heart rate recovery from, the stress of the running sessions. The major question of interest was whether cross-tolerance between the physiological stress of exercise and the psychological stress of the open-field would develop and be reflected in Runners having a faster rate of adaptation to the novelty of the open-field relative to Matched or Caged Controls.



## METHOD SECTION

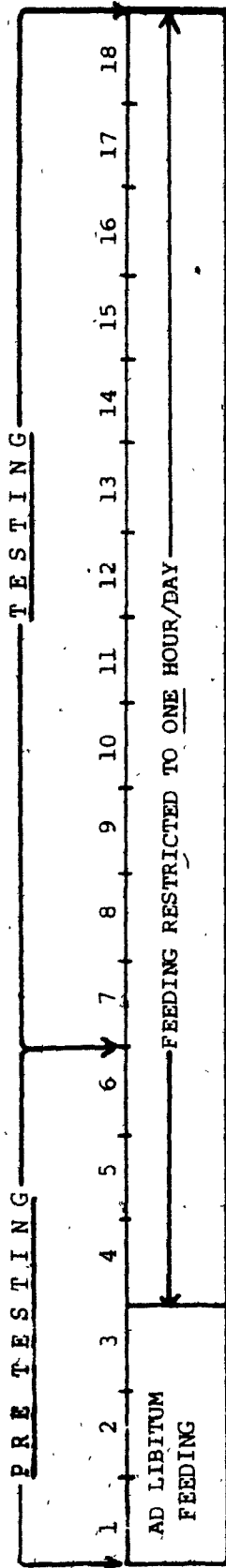
Subjects: Thirty three male Wistar rats ranging from 43-45 days of age and weighing 125-150 grams, served as subjects. Animals were housed in a reverse cycle room (12 hrs. of dark starting at 10 a.m.) where they were initially paired in standard stainless steel lab cages for one month before being individually housed.

Apparatus: Standard Wahmann activity wheels were used with 10"x6"x5" side cages and sliding partitions. Each activity wheel was fitted with a micro switch, a flashing light (connected to the micro switch) mounted in front of the running rat, and a brake which allowed the wheel to rotate only in one direction. Stationary running wheels were of the same dimensions as the activity wheels but there were no side cages used. A light, mounted on each stationary wheel, was coupled electrically to a specific activity wheel so that when the light mounted on the activity wheel flashed, so did its twin mounted on the paired stationary wheel. The lights were wired to flash with each 360 degree revolution of the activity wheel. An Esterline Angus event recorder, Style number 90M, as well as counters, were used to measure the number and patterns of revolutions run in the wheels. Grass Instrument Model 7 Polygraph with alligator clip leads was used to record heart rates (EKG). All subjects had subcutaneous electrodes permanently implanted on either side of their thoracic cavities for this purpose. A three tower unit made it possible to record the EKG's on three animals simultaneously while at the same time reducing the movement

artifact. The towers were nine inches apart and 16" above the base, with each tower platform being a box measuring 9"x3"x1.5". The open-field used for activity measures, was 36"x36"x12" high, made out of plywood. The floor was divided into 6" squares and painted in a cream and black checkerboard design. The sides were painted a cream color as well. Carrying boxes were used to transport animals, eight to nine at a time, from home cage to testing rooms. These were fitted with opaque covers to keep subjects in the dark. Both test rooms were dimly lit by 25 watt red, translucent bulbs. Room temperature was kept constant at 68 degrees Farenheit.

Procedure: Pre Testing. All subjects were handled and weighed daily during which time they were grouped together (see Figure 1). Standard Purina rat chow and water were provided ad libitum for the first three weeks, after which access to food was limited to one hour per day. At the conclusion of that hour, a one inch food pellet was left for each rat. Water was provided ad libitum throughout the experiment.

Three weeks following the implementation of the restricted feeding schedule, the mean weight for each subject was calculated from the last five consecutive weights recorded. Based on these weights, subjects were then divided into three equal groups (n=11), having mean group weights of 265 grams, 266 grams and 265 grams. These were then randomly labeled either "Runners", "Matched Controls" or "Caged Controls". Testing squads, consisting of one member from each of the experimental groups, were formed to control for the possible effects of time of day on



**FIGURE 1** Feeding and Weight Procedures Throughout 18 Week Program

performance, as well as a means of maintaining a constant Runner/Matched Control comparison. All squads were administered the experimental procedures sometime between the hours of 10:00 am and 3:00 pm. Times of treatments were rotated within this period since peak activity is supposed to occur during the first hours of darkness (Zucker & Stephan, 1973) and all squads could not be processed within such a restricted period of time. Since each squad was consistently comprised of the same members from each of the three groups, for all experimental procedures, the time factor was again controlled for. Runners and Matched Controls were given four days to become familiarized with the experimental routines and equipment to be used (spending 10 minutes per day in the activity or fixed wheels). Experimental procedures were carried out during the week (Monday to Friday), but animals were still maintained on the restricted feeding schedule on non-testing days.

General Testing Procedure The testing period lasted a total of 12 weeks (See Figure 2). For the first five weeks the Runners' speed (number of wheel revs./unit time) and duration of running was progressively increased to one hour per day, five days a week. Matched Controls' time spent in their stationary wheels increased at the same rate as that of the Runners; though no restriction was put on the degree of activity they performed. In the fifth week all subjects had electrocardiograms (EKG) recorded for the first time. This measure was continued weekly for six weeks. Four different readings were taken per session: Baseline, 2nd Stage (Immediate post run for Runners), 3rd Stage (15 minute post run for Runners), and 4th Stage (30 minute post

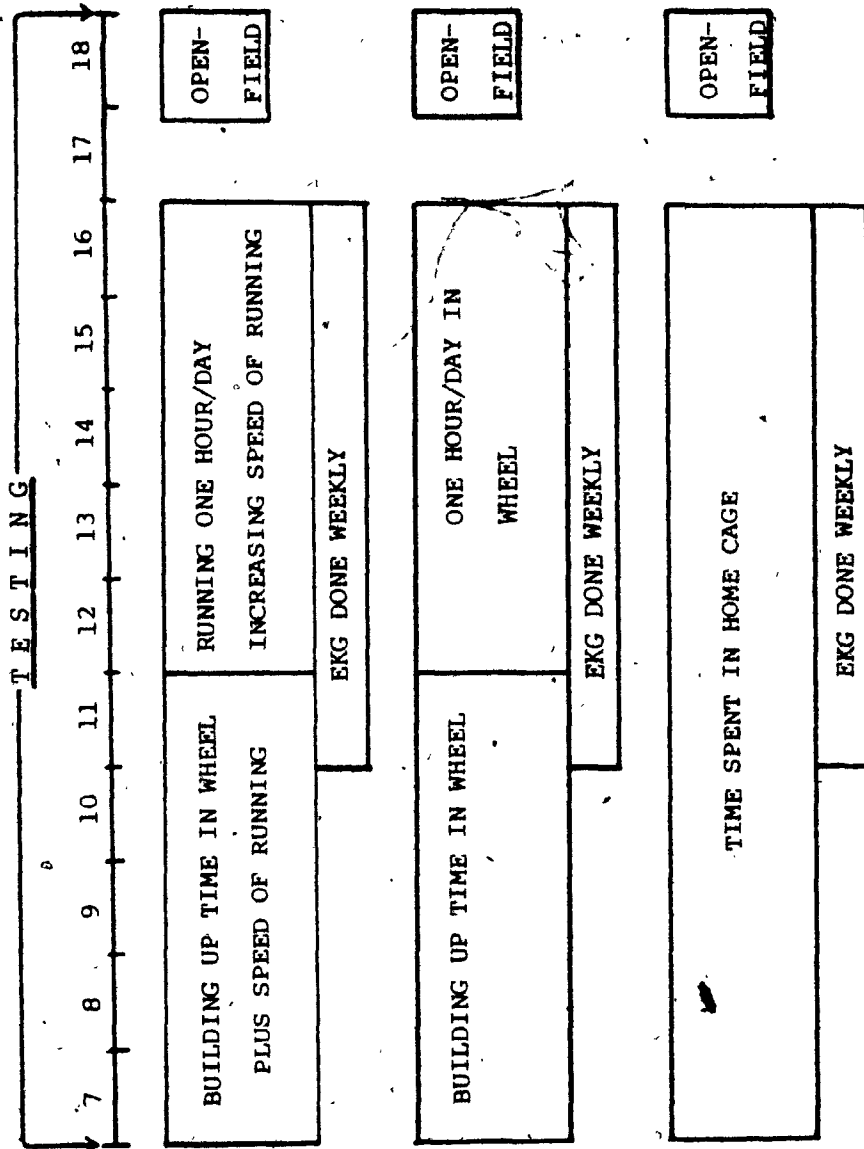
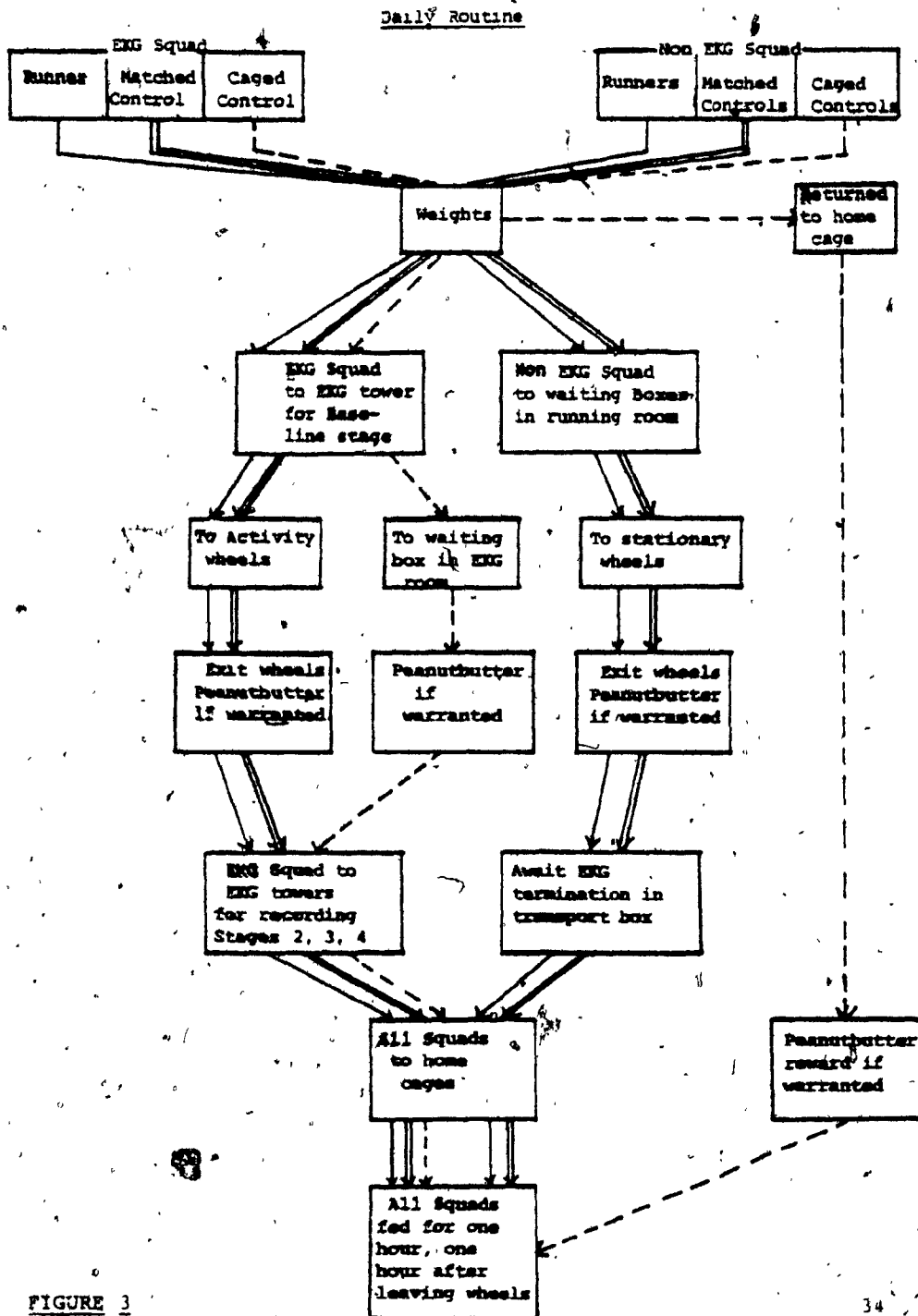


FIGURE 2 . General Testing Procedure

run for Runners)2. The day of the week that squads were tested was rotated. Until EKG measures were begun, Caged Control animals remained in their home cages when the Runners and Matched Controls went to their wheels, though they had remained with their group members while the weights were being taken. During the 12th week all squads were exposed to two 10 minute sessions in the open-field3.

Specific Test Procedures Testing began within one hour after the onset of the dark cycle (between 10-11 a.m.) (See Figure 3). Squads of animals were first weighed and then transported in a darkened, covered box to the already dimly lit testing rooms. The animals designated to have EKG's done that day went to the EKG room where they were placed in the towers for 15 minutes before baseline readings were done. The other animals waited in the running room in individual boxes for that same period of time. Animals in towers had their EKG leads attached five minutes before measures were to be recorded. Ten second segments were recorded and extrapolated to beats per minute. If electrical interference occurred due to movement in any one of the subjects, another 10 second segment was recorded for all three. On termination of the baseline recordings that squad of animals was moved (again in the darkened transport box) to the running room. All Runners were placed in the side cages of the activity wheels with the partitions separating them from the wheels, closed. Matched Controls were placed in their fixed wheels, then the partitions were slid to the side of the running wheels allowing the Runners access to their wheels, and closed behind them so



**FIGURE 3**

Daily Routine For All Test Squads Where Each Squad Is Comprised Of One Member From Each Of The Three Groups (Runners, Matched Controls, and Caged Controls) And This Arrangement Remains Throughout The Experiment

they could not return to the side cages until the designated time for running was completed. Counters and event recorder were activated as soon as partitions were closed. Peanut butter was given as a reinforcer for running immediately on termination in the wheels. If an animal had performed its average number of revolutions or more for that period of training (for example, it may have averaged approximately 800 revolutions per hour, therefore must equal or better that score), it received this reward. If performance was not up to par the reward was not given. Both control groups received the same reward if their squad Runner had merited it. Thus animals learned to expect this because of the repeated presentations over time. This was demonstrated by the high level of activity directed towards the peanut butter being presented to them (most animals would lunge forward and attack the reward). Just before termination of the running period, the Caged Control animal, waiting quietly in the dimly illuminated EKG room, was given a peanut butter reward (if warranted) and removed from his waiting box where he was immediately placed in the EKG tower. Leads were connected as before and a 10 second reading was done. The Pseudo Runner was removed from its cage, given peanut butter, if warranted, and immediately transported to the EKG room where it was placed in the tower, leads attached, and a 10 second reading taken. The Runner, in the meantime had still been running. All flashing lights were now fixed in the "on" position signalling, for the animals, the termination of running for the day; the wheel was stopped and counters for all Runners stopped. If the Runner designated to have its EKG done had run the appropriate number



of revolutions then it was given peanut butter and immediately transferred from the running room to the EKG tower, where the same EKG procedure was performed. All three subjects remained in their towers with leads attached for the next one half hour until all of the readings were completed. In the meantime, the remaining squads of Runners and Matched Controls were removed from their wheels and given their peanut butter if each squad's Runner had run enough. They were then placed together in the transport box to await the return of the squad having its EKG done. Once readings were completed, all subjects were taken back to their home cages in the darkened transport box where they waited one hour before being fed. Control animals that had waited in home cages, since they were not having EKG's done that day, were given peanut butter if their respective squad Runners had performed adequately.

Open-field testing was done following termination of running on two different days for each subject. Squads of animals were transported in darkness to the running room where they remained in their box to wait their turn. The animal to be tested was put in a smaller darkened box and moved to a novel, brightly illuminated room (usual overhead fluorescent lights). Here the subject remained in the box until just prior to being placed in the field, so that the brightness of the room might add to the stress of the novel condition. The lid was removed and the animal quietly placed in one corner of the field with its nose towards the corner. Emergence Time from that corner square plus the number of inside squares crossed, outside squares

crossed and total number of squares crossed, for the first and second five minutes were recorded. A score was given when both front feet moved into a new square. Defecation and urination were also noted. The second ten minute test session was done two days later following the same procedure, except that the corner square in which the subject was first placed was changed to another corner.

## RESULTS

Analyses of variance were utilized for weight, open-field and heart rate data using BALANOVA Class B design for repeated measures (Herzberg, 1968). Independent variables for each dependent measure are summarized in Table 1; source tables are in Tables 2-7.

Body weight showed a main effect for weeks as can be seen in Table 2, ( $F(9,270)=164.47$ ;  $p<.0001$ ). This reflects an increase over weeks as shown in Figure 4. There was no significant main effect for the group factor and no significant interaction.

Runners, speed and duration of running progressively increased over weeks. This increase occurred for both measures during the first six weeks of the training program and then leveled off for the duration (See Figure 5).

Heart rate showed a main effect for weeks as can be seen in Table 3, ( $F(4,360)=4.07$ ;  $p<.001$ ). This reflects a decrease in heart rate over weeks which can be seen in Figures 6 & 7. There was no main effect for the group factor and no significant interaction between groups and weeks. Heart rate also showed a main effect for stages within sessions shown in Figure 8, ( $F(3,360)=28.99$ ;  $p<.0001$ ). This effect is examined further by using the Scheffé post hoc test (C. Diff.=27.12;  $p<.05$ ), demonstrating a significant increase between the Baseline (habituated) and Stage 2 measures, as well as a significant decrease between those measures of Stage 2 and both Stages 3 & 4.

TABLE 1

Data Analysis Summary Table  
Analysis of Variance: BALANOVA Class B  
Design For Repeated Measures  
Where Factors Listed Represent Highest Level Effects  
Designs, And Anything Lower in The Hierarchy is Assumed

Dependent Variables

Body Weight

Open-field

-Total # of Squares

-Inside Squares

-Outside Squares

-Emergence Time

Heart Rate

Independent Variables

Groups x Weeks

Groups x Stages x Time

Groups x Stages x Time

Groups x Stages x Time

Groups x Days

Groups x Stages x Weeks

R = ▲  
 MC = ●  
 CC = ■

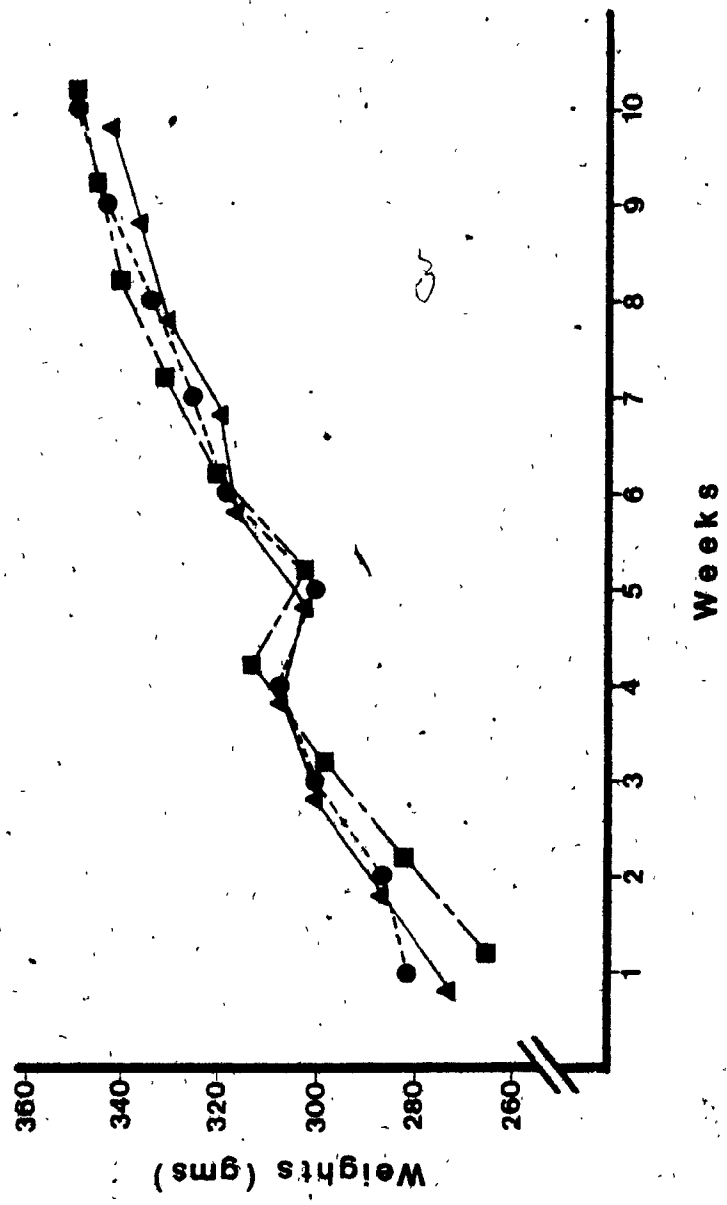
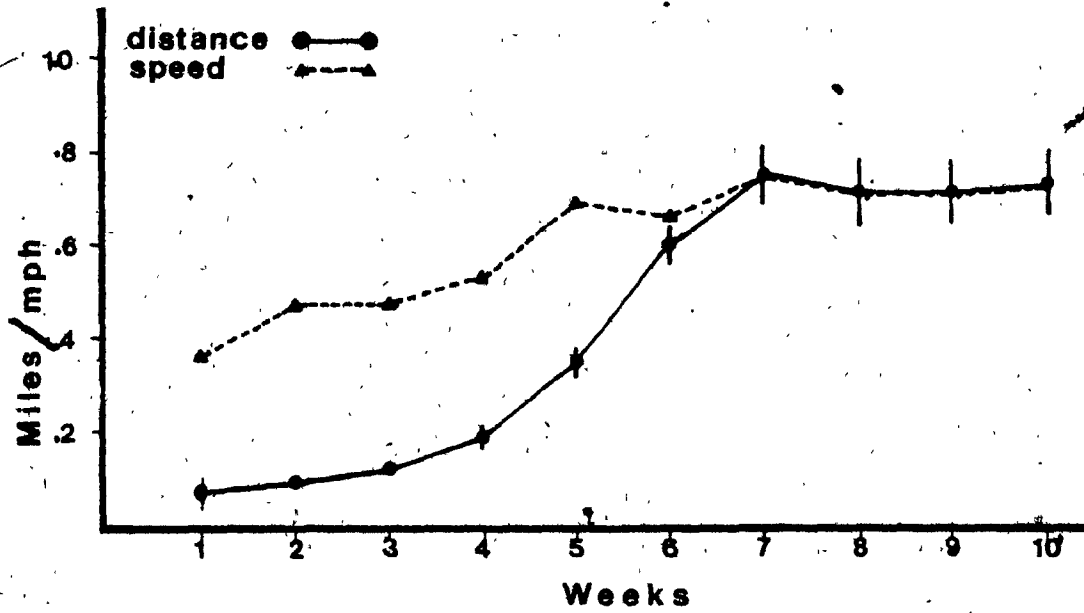


Figure 4 Mean weekly weights over 10 weeks

TABLE 2

Analysis of Variance Source Table For  
Body Weights of All Animals Over Ten Weeks

<u>Source</u>	<u>SS</u>	<u>df</u>	<u>MS</u>	<u>F</u>	<u>p</u>
Groups (G)	865.7	2	432.8	.82	n.s.
Error b	158106.0	30	5270.2		
Weeks (W)	174622.0	9	19402.5	164.47	<.0001
GxW	3130.7	18	173.9	1.47	n.s.
Error (WxS) 1	31851.5	270	118.0		



**FIGURE 5**

Runners, Time Spent In Wheel And Speed Of Running  
Over 10 Week Training Program

TABLE 3

Analysis of Variance Source Table For  
Heart Rate For All Groups Over Last Five Weeks of  
Exercise Program

<u>Source</u>	<u>SS</u>	<u>df</u>	<u>MS</u>	<u>F</u>	<u>P</u>
Groups (G)	31015.3	2	15507.7	1.58	n.s.
Error b	294028.0	30	9800.9		
Stages ("S")	150762.0	3	50253.9	29.00	<.0001
Gx"S"	42805.4	6	7134.2	4.12	<.001
Error (TxS) 1	156033.0	90	1733.0		
Weeks (W)	41590.9	4	10397.7	4.71	<.001
GxW	8488.2	8	1061.0	.48	n.s.
Error (WxS) 2	264938.0	120	2207.8		
"S"xW	9997.2	12	833.1	1.18	n.s.
Gx"S"xW	21791.0	24	908.0	1.28	n.s.
Error ("S"xWxS) 3	254705.0	360	707.5		



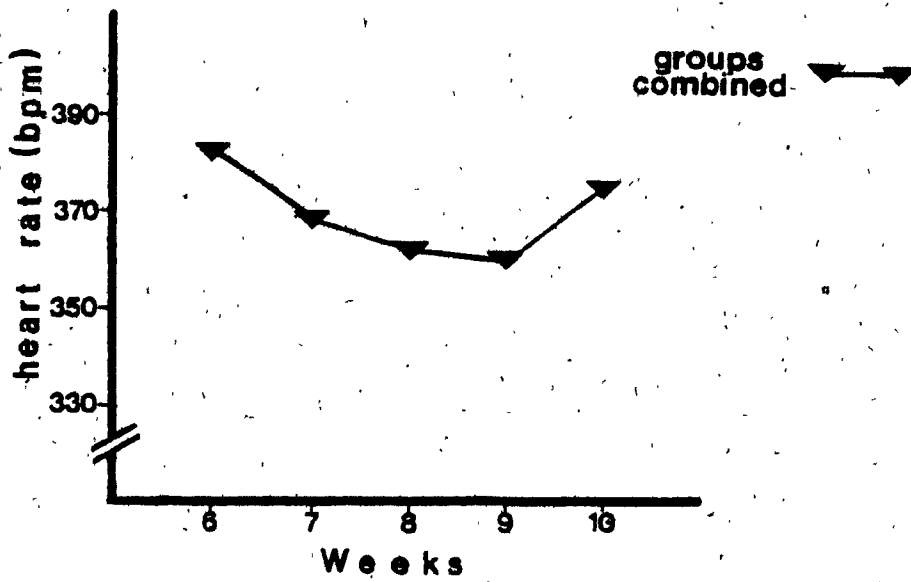
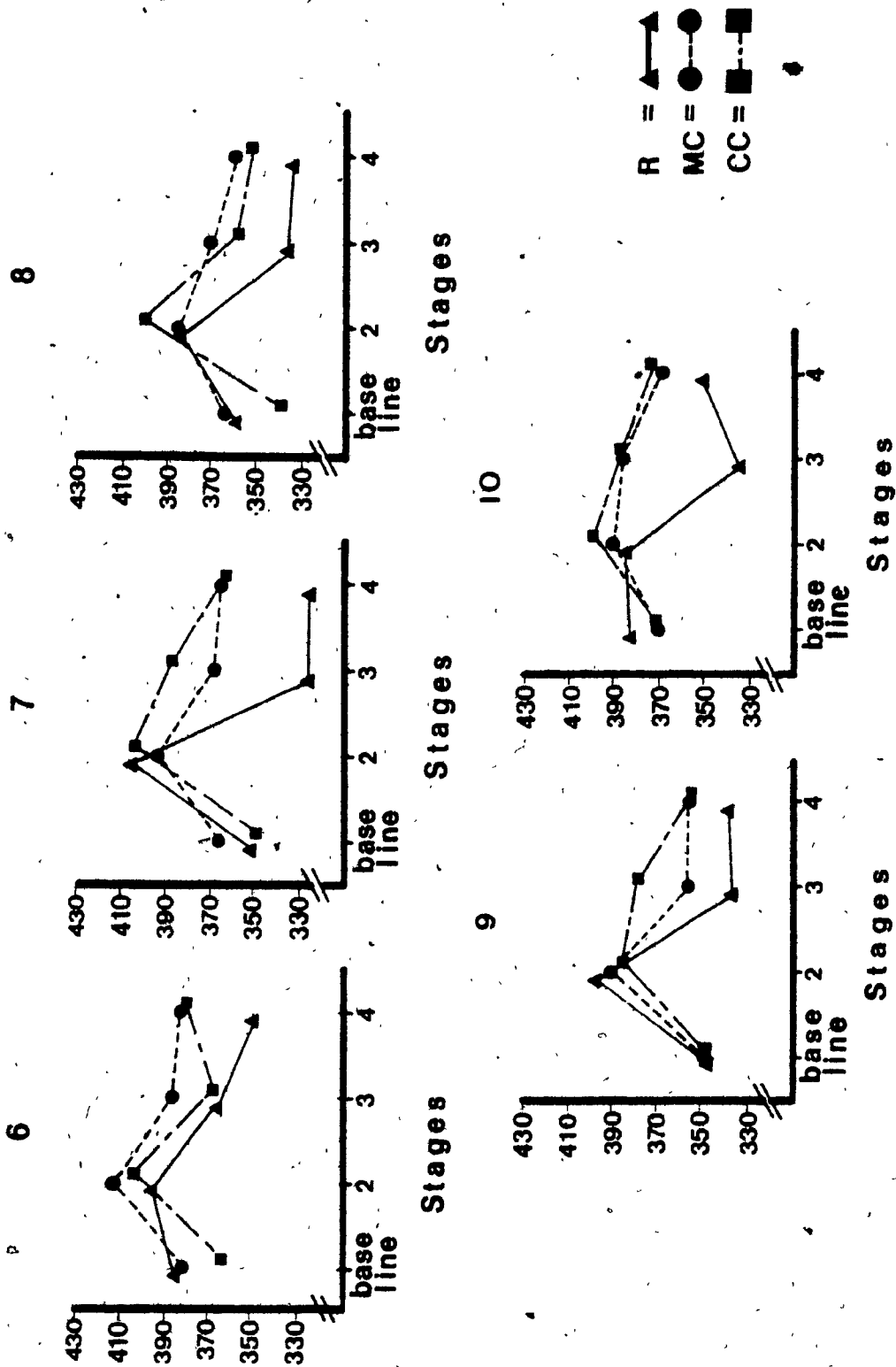


FIGURE 6

Heart rate measures, all groups  
combined over five weeks



**FIGURE 7** Weekly heart rates for all groups from weeks 6-10 of the running program

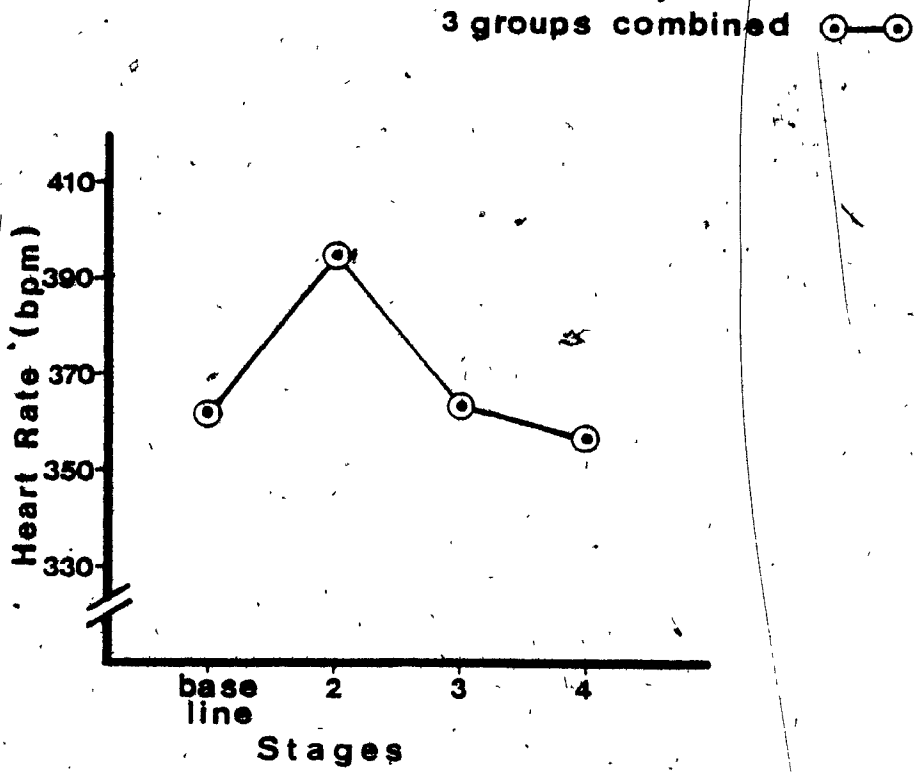
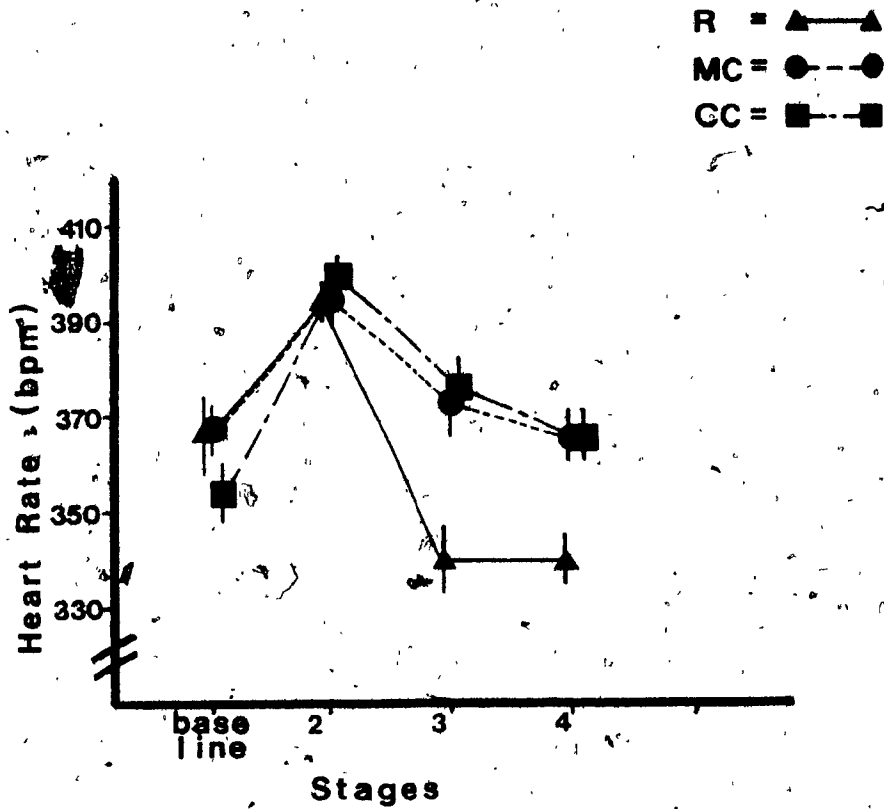


FIGURE 8

Heart rate changes for all groups as a function of stages

There was a Group-by-Stages interaction for heart rate shown in Figure 9, ( $F(6,360)=4.12$ ;  $p<.001$ ). An F-test For Simple Effects was used as a post hoc test (Bruning & Kintz, 1977), showing that Matched Controls' and Caged Controls' heart rates did not differ from each other over stages ( $F(3,360)=.12$ ;  $p<.05$ ). A second F-Test For Simple Effects was computed to compare Runners with the two control groups (Matched and Caged Controls) combined. Results showed Runners' heart rates differed significantly from the combined Controls' ( $F(3,360)=4.48$ ;  $p<.01$ ). Scheffé's post hoc test (Bruning & Kintz, 1977) showed that the Runners, heart rates recovered significantly faster than Controls between Stage 2 and Stages 3 & 4 (C.Diff.=46.92;  $p<.05$ ). While heart rate was below Baseline at Stages 3 & 4 for Runners, this was not statistically reliable.

Total Number of Squares crossed in the open-field showed a main effect for time (minutes) as can be seen in Table 4, ( $F(1,30)=51.46$ ;  $p<.0001$ ). This reflected a decrease in squares crossed from the first to the second five minutes of each day shown in Figure 10. There were no main effects shown for days or treatments and no interactions. Number of Inside Squares crossed showed a main effect for time (minutes) as seen in Table 5, ( $F(1,30)=14.48$ ;  $p<.0007$ ) but there were no main effects for the group or day factors. There was a significant interaction between days and time (minutes) as seen in Table 5, Figures 11 & 12, ( $F(1,30)=6.15$ ;  $p<.02$ ). A Scheffé post hoc analysis (C. Diff.=7.99;  $p<.001$ ) showed that animals crossed more inside squares on Day 1 than on Day 2, but

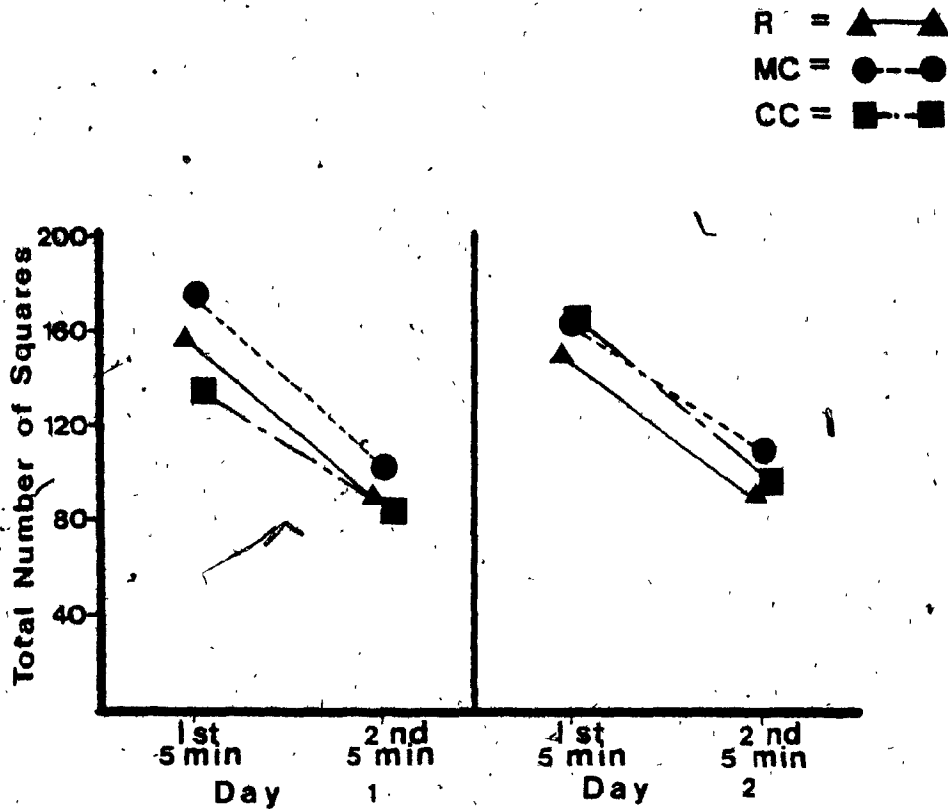


**FIGURE 9**  
Changes in heart rate over stages.

**TABLE 4**

**Analysis of Variance Source Table For  
Total Number of Squares Crossed in The Open-field First  
And Second Five Minutes Over Two Days**

<u>Source</u>	<u>SS</u>	<u>df</u>	<u>MS</u>	<u>F</u>	<u>P</u>
Groups (G)	5274.2	2	2637.1	.31	n.s.
Error	253070.0	30	8435.7		
b					
Time (T)	129469.0	1	129469.0	51.46	<0001
GxT	1296.6	2	648.3	.26	n.s.
Error (TxS)	75481.1	30	2516.0		
1					
Days (D)	315.3	1	315.3	.10	n.s.
Gx"S"	4380.2	2	2190.1	.70	n.s.
Error (DxS)	93958.5	30	3132.0		
2					
Tx"S"	31.0	1	31.0	.34	n.s.
GxTx"S"	3244.1	2	1622.0	1.78	n.s.
Error (TxDxS)	27349.9	30	911.6		
3					



**FIGURE 10**

Total number of squares crossed as a function of minutes within days.

TABLE 5

Analysis of Variance Source Table For  
 Number of Inside Squares Crossed In The Open-field  
 First And Second Five Minutes Over Two Days

<u>Source</u>	<u>SS</u>	<u>df</u>	<u>MS</u>	<u>F</u>	<u>P</u>
Groups (G)	4498.9	2	249.5	.51	n.s.
Error b	14692.4	30	489.7		
Time (T)	2754.6	1	2754.6	14.48	<.001
GxT	243.5	2	121.7	.64	n.s.
Error (TxS) 1	5708.7	30	190.3		
Days (D)	411.3	1	411.3	1.59	n.s.
GxD	1449.2	2	724.6	2.79	n.s.
Error (DxS) 2	7784.3	30	259.5		
TxD	761.3	1	761.3	6.15	<.02
GxTxD	238.6	2	119.3	.96	n.s.
Error (TxDxS) 3	3713.9	30	123.8		



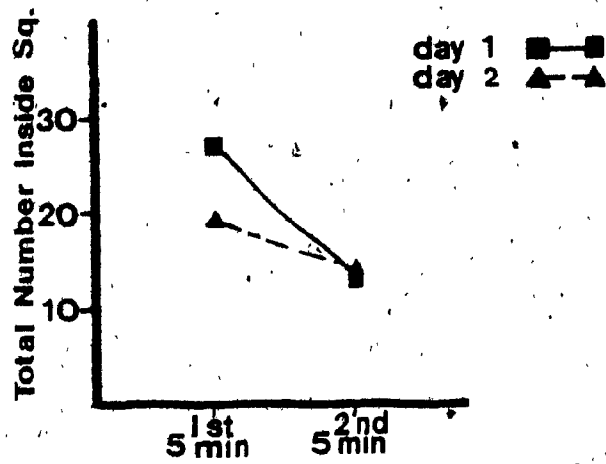
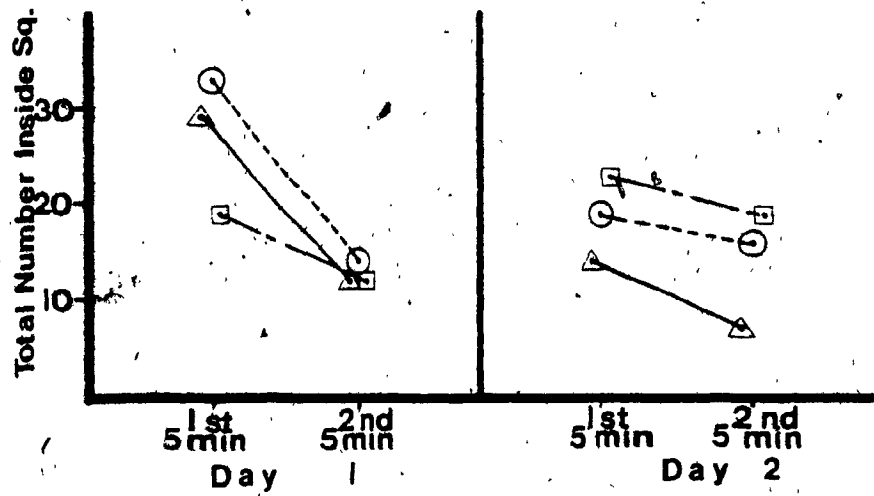


FIGURE 11

Number of inside squares crossed differed as a function of minutes over days

R =  $\triangle$ — $\triangle$   
 MC =  $\odot$ --- $\odot$   
 CC =  $\square$ --- $\square$



**FIGURE 12**

Number of inside squares crossed differed  
 as a function of the interaction between  
 days and minutes

only during the first five minutes of the days. Also, animals on Day 1 significantly decreased their inside squares crossed over time. There was no significant interaction involving treatments. The Number of Outside Squares crossed showed a main effect for time (minutes) as can be seen in Table 6, ( $F(1,30)=69.57$ ;  $p<.0001$ ). This reflects a decrease in outside squares crossed over time for both days as shown in Figure 13. There were no main effects for either the group or day (replication) factors. There were no significant interactions.

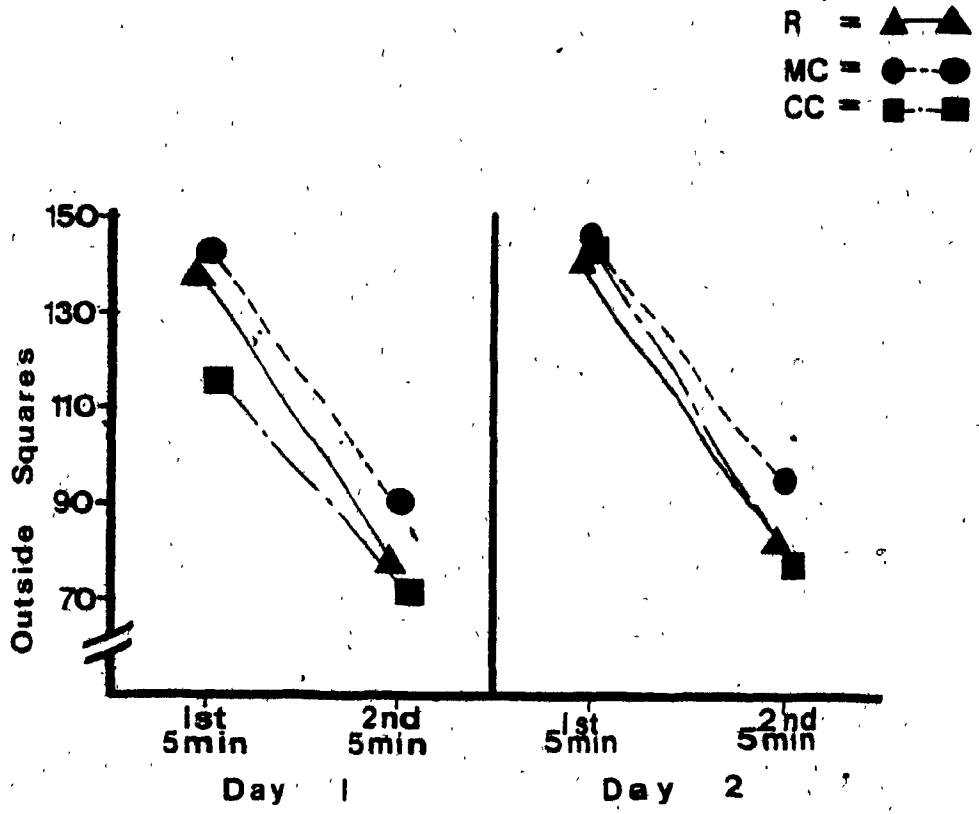
Emergence Time showed a main effect for days as can be seen in Table 7, Figure 14, ( $F(1,30)=22.62$ ;  $p<.0001$ ). There was a group-by-day interaction, seen in Figure 15, where an F-Test For Simple Effects was carried out showing significant differences in performance between the groups on Day 1, ( $F(2,30)=3.70$ ;  $p<.05$ ) and on Day 2, ( $F(2,30)=3.41$ ;  $p<.05$ ). A Scheffé post hoc test showed that these differences occurred between Runners and Matched Controls on Day 1 (C. Diff.=1.19;  $p<.05$ ). Results just failed to reach significance between the performances of Runners and Matched Controls on Day 2, (C. Diff.=1.19;  $p>.05$ ). The differences between Runners and Matched Controls on Day 2 was 1.17. Individual Scheffé tests were done for within group comparisons demonstrating that Runners' Emergence times changed significantly over days (C. Diff.=.96;  $p<.05$ ) while Matched and Caged Controls' times did not. This reflects a decrease in Emergence Time for Runners over days.

Neither urination nor defecation scores changed significantly between treatments or days in the open-field

TABLE 6

Analysis of Variance Source Table For  
Number of Outside Squares Crossed In The Open-field  
First And Second Five Minutes Over Two Days

<u>Source</u>	<u>SS</u>	<u>df</u>	<u>MS</u>	<u>F</u>	<u>P</u>
Groups (G)	5843.3	2	2921.6	.52	n.s.
Error b	167319.0	30	5577.3		
Time (T)	100928.0	1	100928.0	69.57	<.0001
GxT	173.1	2	86.6	.60	n.s.
Error (TxS) 1	43524.9	30	1450.8		
Days (D)	20032.8	1	20032.8	.97	n.s.
GxD	1440.2	2	720.1	.35	n.s.
Error (DxS) 2	62602.0	30	2086.7		
TxD	224.1	1	224.1	.26	n.s.
GxTxD	1065.7	2	532.8	.61	n.s.
Error (TxDxS) 3	26116.2	30	870.5		



**FIGURE 43**

Number of outside squares crossed differed as a function of minutes within days

TABLE 7

Analysis of Variance Source Table For  
Emergence Time In The Open-field Over  
Two Days

<u>Source</u>	<u>SS</u>	<u>df</u>	<u>MS</u>	<u>F</u>	<u>p</u>
Groups (G)	.6	2	.3	.18	n.s.
Error b	47.5	30	1.6		
Days (D)	26.7	1	26.7	22.62	<.0001
GxD	14.8	2	7.4	6.35	<.005
Error (DxS) 1	35.5	30	1.2		

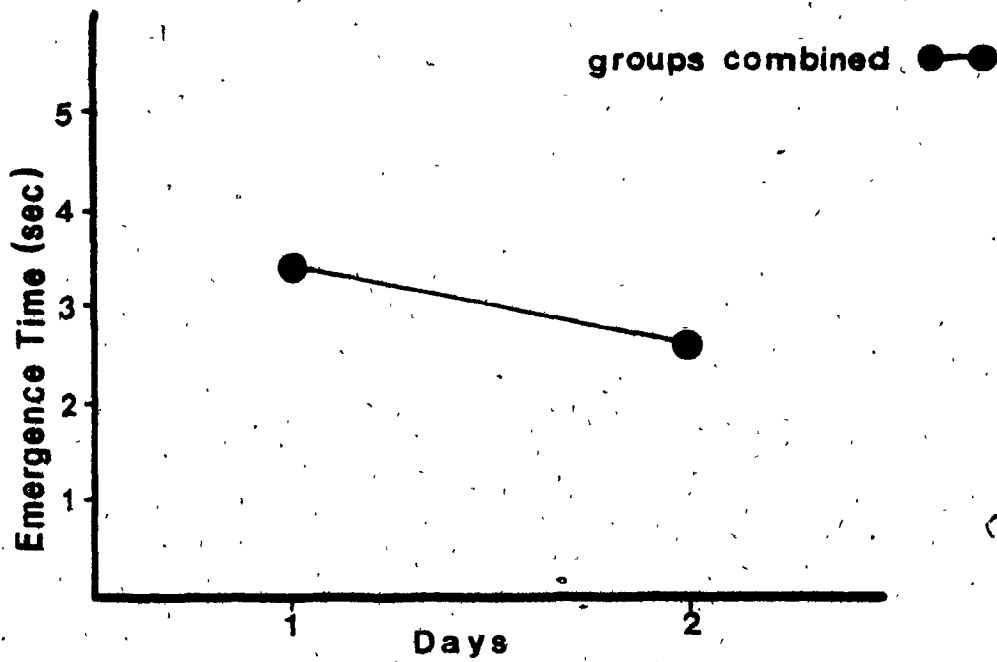


FIGURE 14

Emergence time in the open-field  
over days, groups combined

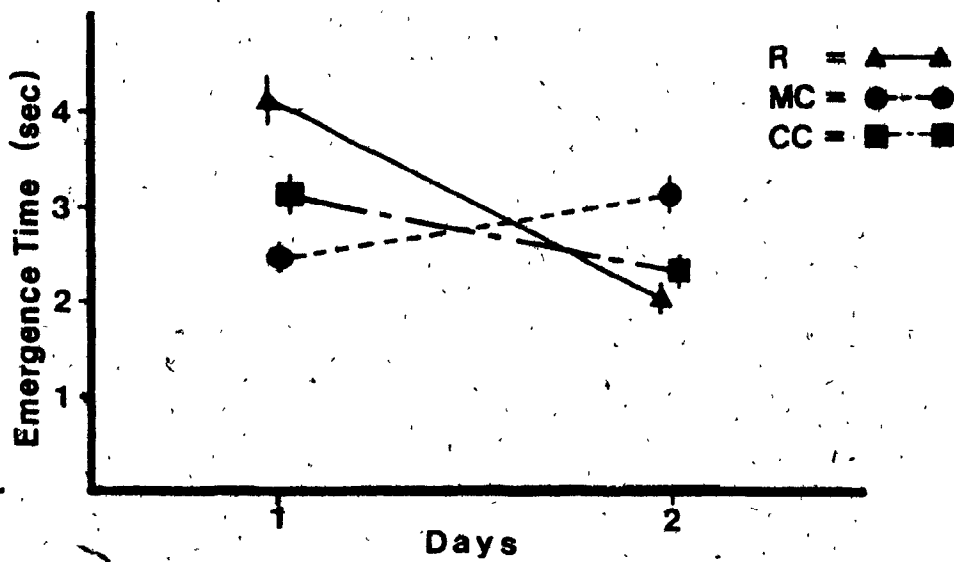


FIGURE 15

Emergence time in the open-field,  
for all groups, over days



and there were no significant interactions.

## DISCUSSION

The present study shows that rats can improve in cardiovascular fitness with a food-rewarded program that contains no additional stressors such as shock or motorized equipment (activity wheels, tread mills). Whether this improvement in cardiovascular fitness influences measures of emotionality is less clear. While Runners did show more rapid habituation to one of the several open-field measures, other open-field scores were inconclusive.

Heart rates increased for all groups between Baseline and Stage 2 of testing. For the Matched and Caged Controls, the source of heart rate increase was due to either handling, reward expectancy, or reward, here after to be defined as psychological. Runners, on the other hand, experienced these same psychological stimuli (handling, expectancy or reward) plus the physiological effects of running, just prior to EKG taking. It is impossible to know to what degree the increase in heart rate of Runners was due to these psychological factors and to what degree the increase was due to running. This problem has arisen because Runners never had their EKG's recorded without the confound of running and thus their responsiveness to handling, expectancy or reward alone was not determined. If running contributed to the heart rate increase in the Runners, then the psychological factors might have had less of an impact on this group than on the two control groups since the total heart rate was the same for all groups. On the other hand, heart rate may be

additive, thus the possible contribution of running to heart rate increase would not necessitate a decreased influence of psychological factors for that measure. If this were the case then, presumably, fitness protected Runners from the effects of the psychological factors which elevated heart rate in the other two groups. On the other hand, if the psychological factors had equal impact on all three groups of animals, then running contributed nothing to the heart rate of Runners. This is possible since the intensity of running had not been sharply increased during the exercise program. Thus animals may have been able to adapt to the level of intensity of exercise provided, producing a minimal increase in heart rate.

Runners recovered significantly faster than both Matched Controls and Caged Controls from the elevation in heart rate, whatever its cause. This is a fitness effect which seems to be related to the exercise regimen (Keller, 1980). To the degree that the increase in heart rate of the Runners does reflect a response to exercise, the heart rate recovery reflects a simple tolerance to exercise stress. On the other hand, to the degree that the increase in heart rate in Runners reflects a response to the psychological factors of handling, expectancy or reward, and not to running itself, the accelerated recovery of Runners reflects a cross-tolerance between these psychological factors and the physiological stress of exercise. Thus it is possible that exercise reduced the response to psychological stress. If so this could have occurred in one of two ways: either it made Runners less sensitive in their peak response to psychological,

factors, or it made them capable of more rapid heart rate recovery. Whether the fitness minimized peak impact or maximized recovery requires further research, as does the question of whether the heart rate responses to psychological factors were due to the handling, the expectancy, or the reward.

It is difficult to evaluate how effective the running program was since EKG's were not begun at the onset of the program due to unforeseen equipment problems (see footnote<sup>1</sup>) and because heart rate was never measured for Runners in the absence of running. It seems unlikely that the running at the end of the program was particularly stressful, since Runners' heart rates did not exceed those of the control groups. Yet, Runners might have shown an initial increase in heart rate during the early part of the program, which by the time EKG measures were begun, would have disappeared due to developing fitness. There is another possibility to be considered. Running at the end of the program might have been stressful but heart rate measures in Stage 2 might not have reflected this because heart rates had already dropped significantly by the time EKG equipment was hooked up. Barnard, Duncan & Thorstensson (1974) have found that heart rate can significantly drop within five to seven seconds after termination of exercise. Thus, it is impossible to tell precisely what factors the heart rate response for Runners was composed of. It is also possible that exercise still had some effect on the heart rate response of Runners at the end of the program since their heart rate response to the psychological factors might have been diminished due to the development of cross-tolerance. This cannot be strongly emphasized however,

since there could have been an interaction effect between the exercise and psychological factors. The faster heart rate recovery (what ever its cause) shown by Runners at the end of the study would seem to support the idea that the program was effective to some degree. Scheuer & Tipton (1977), found that physically fit individuals' heart rates recovered faster than unfits'. Running would not lead to faster recovery by the end of the program if it did not have some significant effect during the program. It seems most plausible that this effect represented, at least in the early phases, a cardiac challenge of some sort. In future studies, the heart rate response to exercise should be monitored earlier in the program.

Open-field scores in general were not different across treatment groups. That is, running did not affect number of squares crossed, whether inside squares, outside squares, or total number of squares are considered. The open-field situation appears to have been an inadequate stressor for the purpose of this experiment, since there was no increase in activity after initial exposure. Scores actually decreased monotonically over time under the present conditions. When the open-field is clearly stressful, the initial period is one in which freezing, urination and defecation are high while activity is low. In subsequent periods urination and defecation would typically decrease while activity increases. Walsh and Cummins (1976), in their critical review of the open-field test, have described various findings which both support and contest this view. In the present study initial freezing and subsequent increase in

activity were not seen; exploration was high from the start and decreased progressively. A more threatening open-field, perhaps better lighted, or possibly where the animals had previously been shocked, might have provided a more adequate psychological stress for testing the present hypothesis.

One open-field score, Emergence Time, did reflect more rapid habituation in the Runner group. This fact suggests that further tests with a more stressful psychological variable may be fruitful. Interestingly, emergence times in the present study (1-4 seconds) were much shorter than those recorded in other studies (one or more minutes: Tharp & Carson, 1975). If a more stressing open-field condition were used and longer emergence times were produced, differences in groups' emergence times might have become more apparent. In view of the fact that in the present experiment the open-field test was generally insensitive in all of its measures except for Emergence Time, and since Walsh and Cummins (1976) have reported inconsistencies in results when this test has previously been used, another psychological stressor might be preferred to the open-field such as heart rate response to a sudden loud noise, or emergence time after a loud noise or restraint (measuring hypothermia).

Data from the present study suggest that this paradigm may still be worth pursuing. If reliable fitness could be established with refinements of this paradigm, it might be a better analogue of human fitness effects than others which are currently available (Harpur, 1980), since it does not utilize punishment such as shock or motorized running equipment to

motivate the animal. Thus a true measure of fitness would be achieved without confounding effects of the stress of running with the stress related to those procedures used to motivate the animals to run. Several of the weaknesses discussed here could be readily reduced in future studies thereby allowing better evaluation of this potential analogue of human fitness.

### Footnotes

Footnote 1 Heart rate measures were begun at this late stage because of unforeseen problems arising with the apparatus originally to be used. This less invasive means of measuring heart rate, by using a tail clip, was found inadequate due to a movement artifact. Thus subcutaneous electrodes had to be implanted at the last moment.

Footnote 2 Only four readings were used because there was data missing for two additional measures (those recorded at five and ten minutes post run).

Footnote 3 The eleventh week of testing was used to collect data on serum lactic acid levels which were subsequently stolen and thus are unavailable.



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