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Exercise Withdrawal"

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ABSTRACT

Title of Thesis: Physiological and Mood Changes Induced by
Exercise Withdrawal

Ali A. Berlin, Master of Science, 2004

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Participation in regular exercise has been associated with decreased prevalence of depressed mood, whereas transient periods of reduced activity result in decreased fitness. However, most research in these areas is limited by cross-sectional designs precluding inferences about causality. The present study examined the effect of systematically controlled withdrawal of high activity levels on psychological measures and fitness. It was hypothesized that decreases in fitness level would contribute to the development of negative mood following withdrawal of high activity. Regularly exercising participants (N=40) were randomly assigned either to withdrawal of high activity or continued usual high activity levels for two weeks. Exercise withdrawal resulted in increased negative mood ($p < 0.01$), and these increases were correlated with decreases in fitness level ($r = 0.39$, $p = 0.014$). This association became non-significant when statistically adjusting for baseline fitness levels and group condition ($p = 0.12$), suggesting that fitness decline does not fully explain the psychological symptoms associated with exercise withdrawal.

Physiological and Mood Changes Induced by Exercise Withdrawal

by

Ali A. Berlin

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INTRODUCTION

Sedentary individuals are at elevated risk of all-cause and cardiovascular mortality as well as a wide range of other physical and mental disorders (Blair et al., 1996; Meyers et al., 2002). Low physical activity levels are associated with biological and psychological risk factors for cardiovascular diseases. However, most research in this area is limited by cross-sectional designs, precluding inferences about causality (Weyerer & Kupfer, 1994; Mensink, Deketh, Schuit, & Hoffmeister, 1996).

Participation in exercise has been associated with improved mood and decreased stress reactivity, while transient periods of reduced activity (e.g., prolonged bed rest) result in physiological changes, among which are decreased fitness level ($VO_2\text{max}$) and biological changes, such as increased markers of inflammation and coagulation (Convertino, 1997; Crandall, Engelke, Pawelczyk, Raven, & Convertino, 1994; Cruickshank, Golrlin, & Jennet, 1988). However, the naturalistic setting poses limitations to the conclusions that can be reached from these studies because of the possible existence of confounding variables (e.g., initial physical activity level, overweight, and psychological status of participants).

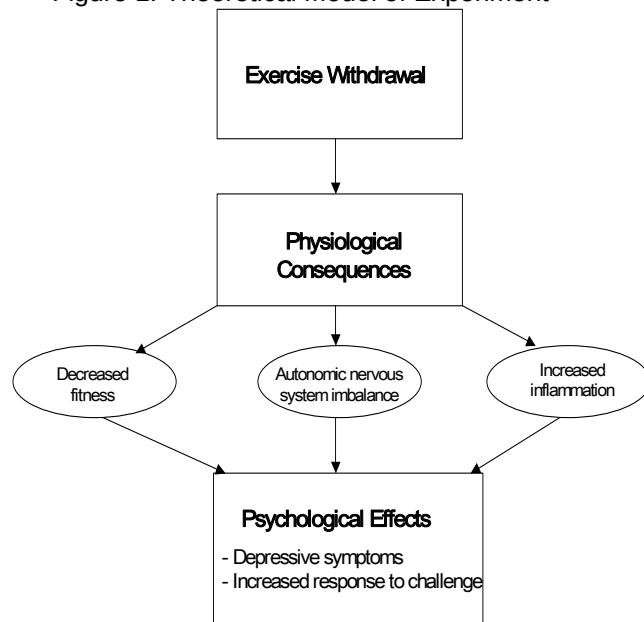
Experimentally controlled exercise withdrawal has well-documented psychological consequences, including negative mood (Chan & Grossman, 1988), but little is known about the possibility of underlying physiological mechanisms explaining these mood changes (Conboy, 1994). The present proposal examines physiological and psychological consequences of exercise deprivation using a longitudinal experimentally controlled design. After a brief

background to the general area of exercise withdrawal, the following sections address: (1) adverse health consequences of a sedentary lifestyle; (2) physiological and biological effects of immobility and exercise withdrawal; (3) psychological consequences of a sedentary lifestyle and exercise withdrawal; and (4) methodological approaches to systematically investigate the effects of reduced exercise levels on physiological, biological, and psychological measures.

Background

Psychological consequences of voluntary or involuntary (i.e., injury-related) exercise deprivation include depressive symptoms, anxiety and increased stress reactivity (Chan et al., 1988; Conboy, 1994; Mondin et al., 1996; Morris, Steinberg, Sykes, & Salmon, 1990; Szabo, 1995). These symptoms adversely affect quality of life, but generally fail to reach diagnostic criteria for psychological disorders. It is not known to what extent these psychological consequences may reflect the physiological and biological effects of exercise withdrawal.

Figure 1. Theoretical Model of Experiment



As is shown in the model presented in Figure 1, the present investigation examined whether psychological effects of exercise withdrawal are contingent upon the physiological and biological responses to reduced exercise levels. Specifically, the current project focuses on the effect of exercise withdrawal on decreased fitness as a potential mechanism accounting for subsequent depressive symptoms.

Sedentary behavior is defined as engaging in no leisure time physical activity and characterizes 40% of the United States population (United States Department of Health and Human Services, 1996). Physical activity is defined as the state of being active, or as energetic action or movement (Pollock et al., 1998). Some investigators consider “exercise” the actual activity of the activity of exerting your muscles in various ways to keep fit whereas “physical activity” is the extent to which an individual engages in any form of exercise or movement (i.e., an index of sedentary lifestyle) (Caspersen, Powell, & Christenson, 1985). Because of the semantic overlap between these definitions, the terms exercise and physical activity are used interchangeably (Pollock et al., 1998). In the present investigation, high physical activity is defined as present if an individual exercises for at least 30 minutes three times per week over a period of six months.

1. Adverse Health Consequences of a Sedentary Lifestyle

Sedentary individuals are at excess risk of mortality compared to

physically active persons, with risk estimates ranging from 1.2 to 2-fold (Meyers et al., 2002). For example, the relative risk of a sedentary individual developing coronary heart disease is 1.8 times greater than an active person (in a follow-up period of 15 years) (Sesso, Paffenbarger, & Lee, 2000).

Evidence suggests a dose-response relationship such that lower physical activity levels are related to increased all-cause and cardiovascular mortality (Kohl, 2001). As the frequency and the intensity of physical activity increase, the rate of all-cause and cardiovascular mortality decrease (Neuberger et al., 1997; Sesso et al., 2000; Stampfer, Hu, Manson, Rimm, & Willett, 2000; Stampfer et al., 2000). Sedentary individuals also are at a greater risk for developing other disorders, including Type II diabetes and rheumatoid arthritis (Ronnemaa, Mattila, Lehtonen, & Kallio, 1986; Uusitupa, 1996).

These adverse health consequences of low physical activity purportedly result from biological and physiological consequences of reduced exercise levels.

The next section reviews the relevant literature on the physiological and biological consequences of the withdrawal of exercise.

2. Physiological and Biological Effects of Reduced Exercise Levels

Physiological indicators of fitness: Aerobic capacity is an important component of physical fitness because it reflects the overall functional capacity of the cardiovascular and respiratory systems (Mitchell, Sproule, & Chapman, 1958) and the ability to carry out prolonged strenuous exercise (Taylor, Buskirk, &

Henschel, 1955). From a health perspective, good cardiorespiratory fitness has been shown to reduce the risk (in adults) of hypertension, coronary heart disease, obesity, diabetes, and some forms of cancer (Blair et al., 1989; Blair, Kohl, Gordon, & Paffenbarger, 1992).

Fitness levels can be operationalized by examining VO_2max , the maximum amount of oxygen an individual can use. Objective fitness levels of sedentary individuals are lower than active individuals (as measured by VO_2max). Bed rest reduces fitness level, depending on the duration of confinement (Convertino, 1983) and initial fitness and health status (Convertino, 1997). A 26% reduction in VO_2max following 21 days of bed rest has been documented (Saltin et al., 1968). Conversely, increases in VO_2max -defined fitness by 3-4% can be achieved by a 6-week exercise training program (Carter et al., 2000) and fitness increases of 16% have been reported after a 16-week exercise training program (Pickering et al., 1997). A detailed description of methodologies regarding fitness is presented on page 29.

Exercise deprivation (withdrawal) studies examining physiologic measures other than VO_2max (e.g, muscle tension) have revealed minimal differences between control and experimental exercise withdrawal conditions (Tooman, Harris, & Mutrie, 1985; Szabo & Gauvin, 1992). Tooman, Harris, and Mutrie (1985) examined 40 runners deprived of running for 2 days. After the second day of deprivation, fitness was operationalized as electromyographically-determined muscle tension at rest. No changes in muscle tension were detected from baseline to exercise deprivation. Szabo and Gauvin (1992) reported a

study with negative findings on fitness as assessed by exercise VO_2max using a 1-week exercise deprivation paradigm among 24 college students. Maximal aerobic power, VO_2max , was assessed during a standard step test. No statistically significant effects of exercise withdrawal were observed on the estimated VO_2max (from 42.1 ± 1.74 mL/kg/min to 42.77 ± 1.81 mL/kg/min). The negative studies are characterized by a relatively short duration of exercise deprivation, 2 days and 1 week, respectively. Longer periods of exercise withdrawal may reveal more pronounced physiological effects. For this reason, 2 weeks of exercise withdrawal in individuals who engage in regular exercise was examined in the present study. The relationship between the hypothesized change in fitness level and subsequent psychological consequences of exercise withdrawal are the primary focus of the present work.

Autonomic nervous system: The balance of the sympathetic and parasympathetic nervous systems plays an important role in cardiovascular homeostasis. Heart rate variability has been used as an indicator of sympathetic-parasympathetic balance. Decreased heart rate variability (respiratory sinus arrhythmia) reflects a primary decrease in parasympathetic nervous system and a shift towards increased sympathetic activity (Dekker et al., 2000; Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996).

Regular exercise, as defined by the American College of Sports Medicine guidelines (Pollock et al., 1998), is associated with greater heart rate variability,

whereas sedentary lifestyles and reduced exercise levels are related to low levels of heart rate variability. Trained athletes commonly have bradycardia (associated with increased heart rate variability) which is probably caused by increased vagal activity and decreased sympathetic activity (Bryan, Ward, & Rippe, 1992; Smith, Hudson, Graitzer, & Raven, 1989).

Prolonged bed rest has pronounced effects on physiological parameters. Heart rate variability is reduced after bed rest, with occasional increased resting heart rate (Crandall et al., 1994). Heart rate variability assessments suggest a primary decrease in parasympathetic tone (vagal withdrawal). As presented in Figure 1, a decrease in heart rate variability would predict an increase in depressive symptoms and increased response to challenge. The present study obtained assessments of heart rate variability, but this thesis primarily addresses fitness (assessed by $VO_2\text{max}$) as the physiological parameter of interest, hence results related to heart rate variability are beyond the scope of this thesis.

Inflammation and coagulation: Increasing evidence supports the role of low-grade inflammatory processes in cardiovascular disease progression (Libby, 2002b). Coagulation factors play a primary role in acute coronary syndromes as well as gradual atherosclerotic processes, which cause atherosclerosis (Libby, 2002b). Vessel wall inflammation constitutes a major factor in the development of atherosclerosis, atheroma instability and plaque disruption followed by local thrombosis, that underlies the clinical presentation of acute coronary syndromes (Libby, 2002a). Acute exercise as well as habitual exercise levels are known to

reduce these inflammatory and coagulation factors involved in cardiovascular disease progression.

Markers of low-grade inflammation and coagulation factors are elevated in sedentary individuals (Mattusch, Dufaux, Heine, Mertens, & Rost, 2000; Rauramaa, Salonen, & Seppanen, 1986). Exercise intervention programs in patients at-risk for heart disease result in a reduction of inflammatory markers, including a 35% reduction in serum levels of C-reactive protein, a 58.3% reduction in mononuclear cell production of atherogenic cytokines (IL-1 α , TNF- α , and IFN- Γ) and a 35.9% increase in atheroprotective cytokines (IL-4, IL-10, and TGF- β 1) (Smith, Dykes, Douglas, Krishnaswamy, & Berk, 1999). In a related study, marathon runners were followed for 9 months of training: median levels of C-reactive protein decreased from 1.19 mg/L to 0.82 mg/L, whereas a group of non-exercisers displayed no change during these same nine months (Mattusch et al., 2000). Therefore, regular exercise may have a systematic effect on inflammatory markers.

Evidence also suggests that exercise affects coagulation factors. Regular moderate physical activity in young healthy men and women decreased platelet adhesion and aggregation properties (Wang, Jen, & Chen, 1995; Wang, Jen, & Chen, 1997). Overweight mildly hypertensive men who engaged in low to moderate intensity physical activity displayed reduced platelet aggregability (Rauramaa et al., 1986). However, the time course of these hemostatic changes in response to increased exercise levels is unknown. Therefore, the clinical use of exercise (as compared to medication) has not been endorsed by medical

practitioners.

In response to acute exercise (the most frequently studied area of exercise-related immune system correlates), a rapid interchange of immune cells between peripheral lymphoid tissues and the circulation occurs. The response depends on many factors, including the intensity, duration, and mode of exercise; concentrations of hormones and cytokines; and changes in body temperature, blood flow, hydration status, and body position. Of all immune cells, natural killer (NK) cells, neutrophils, and monocytes (i.e., innate immune system parameters) appear to be most responsive to the effects of acute exercise, both in terms of numbers and function (Rowbottom & Green, 2000). In general, acute exercise bouts of moderate duration (< 60 min) and intensity (< 60% maximal heart rate) are associated with fewer perturbations and less challenge to the immune system than are prolonged, high-intensity sessions (Rowbottom et al., 2000). Acute exercise induces a substantial, immediate, intensity-dependent increase in circulating NK cell count, usually with a matching rise of NK cytolytic activity (DeRijk et al., 1997). NK cells are released into the circulation during exercise mainly because of a catecholamine-induced alteration in the expression of cellular adhesion molecules at the vascular lining (DeRijk et al., 1997; Zelazowska et al., 1997). The present study was not designed to examine acute exercise-induced immune system responses because the mood changes following 2 weeks exercise withdrawal are purportedly stable and not limited to the acute exercise response.

Coagulation factors are known to be affected by both chronic and acute

exercise levels. Exercise deprivation or reduced mobility during airline travel is associated with deep vein thrombosis (Cruickshank et al., 1988). It has been hypothesized that thrombosis may be caused by the prolonged recumbency and reduced calf pumping caused by long airplane trips (Bagshaw, 1996). Extreme immobility during airline travel may promote the development of thrombosis (Cruickshank et al., 1988). However, the effects of long-term exercise withdrawal, of high activity levels, on inflammation and coagulation factors are not well understood. It is known that hemostatic measures are related to psychological characteristics particularly those that coincide with reduced physical activity and exercise withdrawal (i.e., depressive symptoms and fatigue) (Kop, Hamulyak, Pernot, & Appels, 1998; Kop et al., 2002b). In the present study, blood samples were obtained, but the evaluation and analysis of inflammation and coagulation parameters is beyond the scope of the present thesis.

In summary, sedentary individuals have physiological and biological characteristics that play a role in the pathophysiology of cardiovascular disease, including reduced fitness, autonomic nervous system dysregulation, and increased pro-inflammatory and coagulation factors. These physiological and biological parameters also respond to exercise withdrawal of shorter duration. As discussed below (section 3), both sedentary lifestyle and exercise withdrawal are associated with a range of psychological changes reflecting negative mood. Although there is substantial overlap in the physiological and biological correlates of reduced physical activity and negative mood states, it is not known which

domain (reduced physical activity versus negative mood) plays a primary role in the development of physiological and biological changes. The present longitudinal experimentally controlled study aimed to clarify the role of one important physiological pathway: the role of reduced fitness in exercise withdrawal-induced mood changes.

3. Psychological Consequences of a Sedentary Lifestyle and Exercise Withdrawal

The predominant psychological correlates of low physical activity levels include depressive symptoms and anxiety. These psychological characteristics are generally in the subsyndromal range (i.e., not meeting diagnostic criteria for mood disorders), but may adversely affect quality of life. Mood correlates of a sedentary lifestyle will be discussed first, followed by changes in depressive symptoms, anxiety, and stress reactivity in response to exercise withdrawal.

Mood Correlates of a Sedentary Lifestyle: Cross-sectional, population based studies have shown an inverse association between exercise and depressive symptoms (Byrne & Byrne, 1993; Kritz-Silverstein, Barrett-Connor, & Corbeau, 2001; Weyerer et al., 1994). Stephens (1988) conducted analyses of surveys conducted in the United States and Canada and found that as physical activity increased, the level of symptoms of anxiety or depression decreased. In individuals performing moderate amounts of physical activity, there was a decrease in depressive symptoms compared to the level of depressive symptoms at first evaluation, and this was particularly true for women and for

older populations (Stephens, 1988). Cross-sectional analyses in a German sample (Weyerer, 1992) of 1536 men and women found that those who reported no physical exercise were 3.15 times more likely to have moderate to severe depression. Similar results were found in a population of older adults in Finland (Ruuskanen & Ruoppila, 1995; Weyerer et al., 1994). However, from these cross-sectional studies, it is not clear whether physical inactivity leads to depressive symptoms or depressive symptoms lead to physical inactivity.

Prospective studies have thus been conducted to determine the direction of this relationship (Dunn, Trivedi, & O'Neal, 2001). For example, the First National Health and Nutrition Examination (NHANES I) (Farmer, Locke, & Moscicki, 1988) follow-up study reported a low level of physical activity was related to a two-fold risk of future occurrences of depression. The reverse has also been documented; individuals at baseline who were depressed engaged in less subsequent physical activity (Dunn et al., 2001)

Prospective studies have also examined whether increases in physical activity lead to reductions in depression. The Iowa 65+ Rural Health Study (Mobily, Rubenstein, Lemke, O'Hara, & Wallace, 1996) found reduced depression scores at a 4-year follow-up among participants who commenced daily walking after having depressive symptoms at the initial intake. An inverse relationship between physical activity and subsequent risk of depression in the Harvard Alumni study also was observed (Paffenbarger, Lee, & Leung, 1994).

These research findings were rooted on population-based examinations of the relationship between physical activity and mood. The paragraphs that follow

focus on experimental examinations of the effects of exercise intervention programs and exercise withdrawal paradigms on mood.

Depressive symptomatology: Exercise programs consistently decrease depressive symptomatology in non-clinical samples (Martinsen, 1990). Exercise also can reduce depressive symptoms in patients with clinical depression (North, McCullagh, & VuTran, 1990; Dunn et al., 2001). Although the most powerful effects of exercise on depressive symptoms have been observed among clinical populations (Babyak et al., 2000), this pattern of results may in part reflect the natural course of symptom remission and accompanying treatments (e.g., pharmacotherapy and cognitive-behavioral therapy) in clinical samples (Scully, Kremer, Meade, Graham, & Dudgeon, 1998). Improvements are observed following both aerobic and anaerobic types of exercise (Scully et al., 1998).

In exercise deprivation studies, depressive symptomatology consistently occurs following cessation of exercise. The most common symptoms reported include loss of energy, fatigue, tension, confusion, lower self-esteem, insomnia and irritability (Conboy, 1994; Gauvin & Szabo, 1992; Harris, 1981; Robbins & Joseph, 1985; Szabo, 1995; Thaxton, 1982). However, the severity of these symptoms does not reach clinical significance.

Exercise withdrawal effects on mood have been examined in a prospective study of athletes. An increase in depressive symptoms following sports injury was demonstrated by an increase on the Zung Depression Scale (increase from 31.27 to 38.00) (Smith et al., 1993). The majority of injuries

examined in the study were classified as “minor,” which signified one week of non-participation in athletic endeavors.

Thaxton (1982) conducted a study with 33 habitual runners. Half of the runners abstained from running for 24 hours while the other half maintained their usual schedule. Reported depressive symptoms (as assessed by the Profile of Mood States (POMS)) were higher in those who missed their run (score in the control group was 1.36 ± 2.80 while in the experimental group, the score was 6.86 ± 7.43 ; higher scores indicating more depressive symptoms). The elevation in depressive symptoms was apparent after only 24 hours of abstinence.

Morris et al. (1990) examined the effects of two-weeks deprivation from running. Forty regular male runners were divided into two groups: a group who continued to run and a group that stopped running for two weeks. Somatic and affective symptoms were assessed using the General Health Questionnaire. During the first week of withdrawal, somatic symptoms (insomnia, anxiety, and feelings of being under strain) were greater in the exercise-withdrawn group. After the second week of withdrawal, mood symptoms developed in the exercise-withdrawn group, including feeling blue and loss of interest in pleasurable activities. The somatic symptoms preceded the affective symptoms in this population. The authors did not investigate this relationship further, but it is possible the development of somatic symptoms predict the development of affective symptoms. The predictive value of somatic symptoms for subsequent cognitive-affective mood changes will be examined in the present thesis.

Anxiety: Exercise has a potential anxiolytic effect on both clinical and non-

clinical populations (Scully et al., 1998). This anxiolytic effect is observed across different measures of anxiety and different exercises performed (Landers & Petruzzello, 1994).

Exercise deprivation has been associated with an increase in anxiousness in general, and specifically state anxiety (Mondin et al., 1996; Robbins et al., 1985). Psychological symptoms of injured runners were compared to non-injured runners and injured runners showed significantly more symptoms of anxiety as measured by the POMS with an increased tension-anxiety subscale score. The prevented runners' scores (12.07) were increased over the continuing runners' scores on tension-anxiety (6.40) (Chan et al., 1988).

Stress Reactivity: Reactivity can be defined as the magnitude of hemodynamic and emotional responses from baseline levels to acute (mental) challenge tasks (see Methods section for various statistical options for operationalization of reactivity) (Krantz, Kop, Santiago, & Gottdiener, 1996; Manuck, Kasprovicz, Monroe, Larkin, & Kaplan, 1989). An improved fitness level purportedly facilitates an individual's ability to deal with environmental challenges (Blumenthal, Fredrikson, & Kuhn, 1990), and may thus result in reduced hemodynamic and emotional reactivity to various exogenous stressors.

Few studies have examined the role of exercise on reactivity to endogenous challenges. In one study, sedentary individuals displayed increased stress responsivity, increased heart rate and blood pressure reactivity to a mental arithmetic task (Blumenthal et al., 1990). Experimental studies on the effect of exercise deprivation on stress responses are rare (Szabo et al., 1992). Minimal

effects of exercise deprivation on the hemodynamic stress response (increased heart rate and blood pressure) to written arithmetic have been reported, but the results were limited by the specifics of the cardiovascular assessments and a possible habituation to the mental challenge test (Szabo et al., 1992). The present study aims to further our understanding of stress reactivity changes among exercise-deprived individuals by using challenge tests that are not susceptible to habituation.

4. Methodological Approaches to Systematically Study The Effects of Exercise Withdrawal on Biological and Psychological Measures

The three most commonly used research designs to study exercise deprivation are: surveys, case-control research, and experimental research. Each of these designs has advantages and disadvantages relevant to the current research questions.

Survey research: More than 50% of the literature on exercise deprivation is based on survey research (Szabo, 1995). There are two basic types of survey research, prospective (i.e., NHANES) and cross-sectional. Prospective designs measure changes in a variable from one period to another, that is, the description of patterns of change over time. Cross-sectional designs do not measure changes over time, but measure different groups of participants at a particular point in time. Both of these survey designs preclude causal inference because of the reliance on self-report data and the lack of experimental manipulation.

Survey research examining low physical activity levels often targets

sedentary populations and defines exercise levels by self-reported daily activity. The major limitation of these types of studies is that they rely on self-report, which may be biased by the participant's knowledge that physical activity is beneficial to one's health. In general, survey research over-estimates the role physical activity on mood because it does not control for the contribution of possible confounding variables that co-occur with physical activity and mood (i.e., overweight). Survey prospective research allows data gathering from a large and diverse population, but it does not allow for experimenter control, limiting the evaluation of causal relationships. The proposed study circumvents such limitations by manipulation of exercise levels, validation of the extent of exercise reduction by objective activity monitors, and prospectively examining its physiological and psychological consequences.

Case-control research: The case-control approach generally compares a high exercise group (e.g., athletes), or a low exercise group (e.g., individuals with injuries) and uses a 'control group' as a reference group. The observed effect sizes of these studies are generally larger than in survey research, and the groups of participants are well described. However, there are limitations to this method. Athletes are a highly selective group and may differ from sedentary individuals on many variables other than activity levels. Injury research is limited by the fact that injuries involve many consequences other than exercise deprivation. For example, pain associated with injury or the lack of mobility caused by the injury may confound the results. In general, case-control studies over-estimate the effects of reduced exercise on mood. Sampling from two

different populations may inflate the chance of finding differences because the groups are different on numerous characteristics that may be related to the variables being investigated.

Experimental research: In order to avoid these sources of bias, the preferred method of studying exercise deprivation is by experimental manipulation of exercise levels. This method allows for evaluation of cause and effect relationships. One limitation of this method is that exercise deprivation for a limited period (i.e., 2 weeks as proposed in this project) may preclude generalizability to clinical populations and individuals with sedentary lifestyles (Szabo, 1995). Another limitation is that participants are not blind to the experimental manipulation. Selection bias also is a limitation in this type of design because people who know they will develop increased symptoms because of withdrawal of exercise will probably not volunteer for this type of research. Also, in past studies there has been no validation or documentation of whether exercise deprivation actually occurred in the experimental group. The present study will use ambulatory actigraphy to monitor adherence to the deprivation protocol (see methods section).

Summary and Hypotheses

The reviewed evidence suggests that low physical activity levels and exercise deprivation are associated with physiological and biological changes, as well as mood and other psychological changes, but the underlying mechanisms and inter-relationships are largely unexplored. It is hypothesized that the

physiological and biological consequences accompanying reduced exercise levels play a role in the psychological consequences of exercise deprivation. The purpose of this study is to examine the time trajectories of the physiological (fitness level), as well as the psychological (depressive symptoms and stress reactivity) changes that occur when regular exercisers are deprived of exercise and the relationships between these time courses.

Although a substantial body of cross-sectional research exists examining the relationship between physical activity and mood, there is a lack of research employing experimental designs. As a consequence, little is known about causal relationships. Along with the paucity of experimental investigations, more research is needed to quantify the physiological and biological consequences of lack of exercise.

The present research examines the effects of exercise withdrawal on mood and fitness levels. The purpose of the study is to determine the time trajectory of the changes in mood and fitness during exercise withdrawal, and to examine whether the mood changes are contingent upon exercise withdrawal-induced changes in fitness. The specific hypotheses for the current study are:

Hypothesis 1: Among regular exercisers, exercise withdrawal (2 weeks) will result in increased negative mood and decreased positive mood.

Hypothesis 2: Somatic symptoms of negative mood (i.e., fatigue, loss of energy) will *precede* changes in cognitive-affective symptoms of negative mood (i.e., sadness, loss of interest) in response to exercise withdrawal. Furthermore,

the magnitude of somatic symptoms will *predict* subsequent changes in cognitive-affective symptoms of negative mood.

Hypothesis 3: Exercise withdrawal will result in increased stress reactivity to mental and physical stress (an increase in blood pressure and heart rate during challenge tasks).

Hypothesis 4: Exercise withdrawal will result in decreased fitness level (VO₂ max and breathing frequency during cycle ergometry).

Hypothesis 5: The magnitude of decreased fitness level following exercise withdrawal will predict the extent of psychological changes: increased negative mood, decreased positive affect, and elevated reactivity to mental and physical challenges.

RESEARCH DESIGN AND METHODS

General Overview

Psychological and physiological measures were assessed in 40 participants randomly assigned to exercise withdrawal or a control condition. As shown in Table 1, participants were tested three times during the protocol: (1) at baseline; (2) at 7 days; and (3) at 14 days.

Table 1. Outline of Experiment

Study Phase	Procedures	Measures
Day 1	Questionnaires	Mood state, fatigue
	Mental Challenge/ Physical Challenge	Hemodynamic responses
	Exercise Test (submaximal)	Fitness level, respiration
	Begin Exercise Withdrawal	
Day 7	Questionnaires	Mood state, fatigue
	Mental Challenge/ Physical Challenge	Hemodynamic responses
	Exercise Test (submaximal)	Fitness level, respiration
Day 14	Questionnaires	Mood state, fatigue
	Mental Challenge/ Physical Challenge	Hemodynamic responses
	Exercise Test (submaximal)	Fitness level, respiration

Participants

This study enrolled participants who were regular exercisers (participating in aerobic exercise at least three times per week for a duration of at least 30 minutes over the past six months) (Pollock et al., 1998). A total of 40 participants

were recruited from the general population by advertising in local newspapers. Twenty were randomly assigned to the experimental exercise withdrawal group and 20 were assigned to the control group. The groups were matched on gender. All of the participants were tested between 6 am and 10 am to control for potential effects of the time of day on the various measurements.

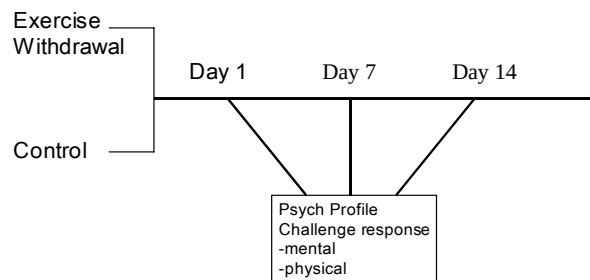
Inclusion criteria were: participating in aerobic exercise at least three times per week for a duration of at least 30 minutes over the past six months (Pollock et al., 1998). Exclusion

criteria were: (1) age <18 or >45; (2) use of anti-inflammatory medication or anti-coagulant medication other than aspirin (to control

confounding in the blood assays; data not presented); (3) history of cardiovascular disease; (4) hypertension (blood pressure >140/90 mmHg); (5) obesity (body mass index (BMI) > 30 kg/m²); (6) currently under the treatment of a psychiatrist or psychologist for a mental disorder; and (7) for military participants: scheduled Physical Performance Testing < 1 month.

An age maximum of 45 was used to minimize the risks associated with the exercise test (Hagberg, 1994) and to reduce potential confounding by age on depressive symptomatology and fitness (Snowdon, 2001; Krause & Clark, 2001; Kurachi et al., 2000).

Figure 2. Model of Experimental Schedule



Procedures

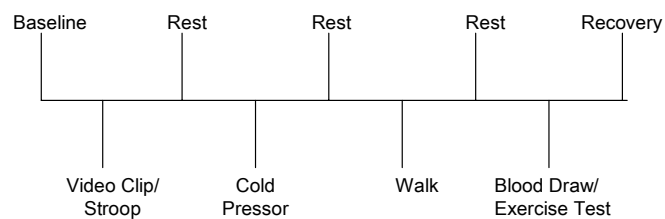
Participant testing and data collection were performed at the Uniformed Services University of the Health Sciences (USUHS, Bethesda, MD). The questionnaires and mental challenge tasks were administered in USUHS Building 28 (supervised by Dr. Willem Kop). The exercise test was conducted at the Human Performance Laboratory (supervised by Dr. Patricia Deuster). After participants gave written informed consent (Appendix A), questionnaires were completed to evaluate demographic information and psychological measures.

The following information was obtained: age, race/ethnicity, height, weight, current medication,

exercise level (Kohl, Blair, Paffenbarger, Macera, & Kronenfeld, 1988), and general

health status. Psychological measures will be described below. After placement of the blood pressure monitor, a 30-minute baseline period (during which questionnaires were filled out: 0-20 min.) was taken to establish baseline hemodynamic measures in a resting condition. Then, a 1-minute video was presented. Film clips from various movies (e.g., Witness, Mrs. Doubtfire, and a train documentary) were used. These clips have been used in previous studies to elicit the emotional response of happiness, anger, or neutral emotions (Waldstein et al., 2000). The film clips were used to add novelty to the Stroop task in order to prevent hemodynamic and emotional attenuation to the repeated

Figure 3. Outline of Study Visit



stressor. Previous work has demonstrated that the film clips do not alter hemodynamic reactivity, while still inducing the three different emotional states prior to the challenge task (Waldstein et al., 2000; Berlin, Newell, Olsen, & Kop, 2004). The subject evaluated one clip per study visit and the order was randomized across subjects. After the mental challenge task, a 3-minute cold pressor was administered.

There were two stressors used in this study to evaluate both mental challenge (Stroop) and physical challenge (cold-pressor) responses to exercise withdrawal. There has been little experimental work on the relationship between stress reactivity and exercise, especially in the exercise withdrawal paradigm. Therefore, it was important to include both a mental and a physical challenge task in order to thoroughly investigate the possible stress reactivity changes induced by exercise withdrawal. Details of these tasks are described below.

Participants were then equipped with an actigraphy wristwatch to be worn for the remainder of the study. Participants walked for approximately 5 minutes to the Human Performance Laboratory where a submaximal exercise test was conducted. A submaximal exercise test was utilized, as the participants performed three exercise tests within a 14-day period. The use of a maximal exercise test was considered to be too physically demanding. The participants randomized to the exercise withdrawal group stopped their normal exercise routine for a period of 14 days.

Approximately seven days following Visit 1, participants returned to the laboratory for the second study visit and completed the same procedures as at

Visit 1. The order and procedures of the tasks remained the same to examine the long-term effects of exercise on physiological and biological measures. The duration of the visit 2 exercise test was shorter to ensure procedural manipulation of exercise withdrawal in the experimental group.

Approximately fourteen days following Visit 1, participants returned to the laboratory and completed the same procedures as at Visits 1 and 2. The duration of the study was set at 14 days because that length of exercise deprivation is optimal to induce mood changes (Conboy, 1994; Mondin et al., 1996; Morris et al., 1990; Mondin et al., 1996). The rationale for participants to return after one week was to enable investigation of the time trajectory of symptoms from study entry (Day 1) to Day 7, rather than merely examining pre (Day 1) versus post (Day 14) effects of 2 weeks of exercise withdrawal.

Measures Obtained during the Study

1. Assessment of Negative and Positive Mood

Negative mood: Consistent with prior studies in this area, negative mood was assessed using the Profile of Mood States (POMS), which has six subscales and a composite score labeled Total Mood Disturbance (TMD). The composite score was calculated by adding the five negative scales (tension, depression, anger, fatigue, and confusion) and subtracting the one positive scale (vigor). Higher POMS TMD values indicate more negative mood (Cronbach's $\alpha=0.65-0.74$; 65 items) (McNair, Lorr, & Droppleman, 1971).

Positive Mood: The Positive and Negative Affectivity Scale (PANAS) was used to assess the positive and negative aspects of mood state (Cronbach's $\alpha=0.84-0.90$; 20 items) (Watson, Clark, & Tellegen, 1988).

Depressed Mood: The Beck Depression Inventory-II was used to assess depressive symptoms (Cronbach's $\alpha=0.92-0.93$; 21 items) (Beck, Steer, & Brown, 1996). This inventory consists of 21 items and the instructions were modified to reflect symptom reports over 1 week (instead of 2 weeks). Beck scores exceeding 10 are considered indicative of potential presence of depression.

Somatic and cognitive-affective symptoms: In order to examine Hypothesis 2 (time trajectories of somatic versus cognitive-affective symptoms), the BDI was divided into two components, based on a previously published factor analysis (Whisman, Perez, & Ramel, 2000). The first factor contains somatic symptoms and the second factor refers to the cognitive-affective symptoms (Helm, Jr. & Boward, 2003). Somatic symptoms of depression are loss of energy, sleep, change in appetite, poor concentration, and fatigue. The cognitive-affective symptoms of depression include sadness, sense of failure, loss of pleasure, guilt, punishment, self-dislike, self-criticalness, suicidal thoughts, crying, agitation, loss of interest, indecisiveness, worthlessness, and irritability (van Diest & Appels, 1991; Whisman et al., 2000).

The Maastricht Interview for Vital Exhaustion (MIVE) was used to assess fatigue levels (Meesters & Appels, 1996), as an additional measure of somatic

symptoms following exercise withdrawal. The interview consists of 23 items and discriminates between cases and controls better than a comparable self-report questionnaire of exhaustion (Meesters et al., 1996). Interviews were tape-recorded to allow reliability measurements. Individuals with 7 or more positive items are classified as exhausted. Copies of the questionnaires and interview are provided (Appendix B).

2. Mental and Physical Challenge Testing

Reactivity to Mental Challenge

Immediately following the video presentation, a Stroop color word computer-based mental challenge task was performed. The Stroop computer task was performed because in previous studies there was minimal habituation to the stressor, which is important because of the repeated exposures to the challenge task inherent in the protocol. Also, a constant level of mental challenge across the three study visits was able to be obtained because the difficulty level of this task automatically increased as the participant's performance improved (Becker et al., 1996; Goldberg et al., 1996).

Participants were asked to press a mouse button (with their dominant hand) representing the display color (blue, red, or green) as fast as they could when color words appeared on the screen. The answers were three color words displayed in three colors. Participants were instructed to respond to the display color of the target word by selecting the correct written word on the lower part of

the screen. For example, if the target word “blue” was presented in red display color, then the three possible answers were the words “blue” displayed in red letters, the word “green” displayed in blue letters, and the word “red” displayed in green letters; the correct response would then be “red” written in green letters. The novelty of the Stroop test was maintained by showing video clips before the task that varied with each of the three study visits. We have previously documented that the preceding film clips reduced habituation to the Stroop test, and that the clips themselves did not result in hemodynamic responses (Waldstein et al., 2000; Berlin, Newell, Olsen, & Kop, 2004).

Reactivity to Physical Challenge

Following the Stroop task, participants rested for 10 minutes. Participants performed a physical challenge that is not prone to habituation, so that across the weeks of the study, the level of physical challenge would be consistent (Zbrozyna & Krebbel, 1985). The participants performed a Cold Pressor Test, in which the hand opposite to the side of the blood pressure cuff was submerged in a bucket of ice water at 4 degrees Celsius (± 1 degree Celsius) for 3 minutes (Patterson et al., 1995). The cold pressor was administered after the mental challenge task in order to circumvent carryover effects of the cold exposure on the mental challenge task.

Reactivity to Exercise

The submaximal bicycle test involved sitting on a stationary bicycle and pedaling at 60 revolutions per minute at four different workloads for 2 minutes at each workload. The starting workload was set at 30 W for women and 60 W for men and was increased by 30 W per stage (Swain & Wright, 1997). The workloads were below the maximal exercise capacity of all subjects, with workloads ranging from very light to moderate to hard (Swain et al., 1997). The maximum heart rate reached was set not to exceed 85% of the participant's age-predicted maximal heart rate ($.85 * (220 - \text{age})$). The test was stopped when 85% of age-based HR was reached, or 8 minutes of exercise was completed. The maximum HR for Visit 2 was set at 70% (instead of 85%) in order to avoid introduction of confounding by exercise during the exercise withdrawal phase.

3. Fitness

The heart rate and workload of the individuals at each stage were used to calculate a measure of fitness (VO_2max). VO_2max is a good indicator of aerobic endurance performance (Mitchell et al., 1958). Ergometry allows the investigator to keep the workload (Watts) constant. The slope of the linear relationship between heart rate and Watts represents the VO_2max of the participant. The magnitude of heart rate increases to the increased workload is inversely related to VO_2max (normal VO_2max values range from 35.0 to 45.0 mL/kg/min) (Shvartz & Reibold, 1990).

In addition to VO_2max , minute ventilation was assessed as an additional measure of fitness. Participants breathed into a spirometer to determine minute ventilation. Specifically, the last 15 seconds of each stage were used to determine the breathing frequency and tidal volume of the participant for each workload. To calculate minute ventilation, breathing frequency (the number of breaths per minute) was multiplied by tidal volume (the amount of air breathed in and out during respiration) (McArdle, Katch, & Katch, 2001).

4. Hemodynamic measures

During rest and challenge tasks, blood pressure and heart rate were obtained at 2-minute intervals using a Critikon Ditmap automated cuff placed on the non-dominant arm. Baseline hemodynamics were determined by averaging the last three resting measures during the rest period. During mental challenge tasks, hemodynamics were assessed every two minutes (the peak of these measurements were taken) and during the 10-minute recovery. This procedure allowed determination of increases in hemodynamic (systolic and diastolic blood pressure, heart rate) measures while adjusting for baseline levels.

Three general strategies for calculating reactivity scores have been described: (1) the aggregated baseline change scores strategy where the entire baseline measures prior to a series of tasks are averaged to compute an overall baseline to subtract from individual task reactivity; (2) the residual change score method, where a regression line is calculated for the relationship between

baseline and task measures and then the residual values from the regression line are used as the reactivity measures; and (3) arithmetic change scores calculated by subtracting the peak task measures from the preceding baseline measures (Kop, Krantz, & Baker, 2001).

Kamarck et al. (1992) support an aggregated baseline across tasks as the proper manner in which to perform a baseline cardiovascular evaluation because the “baseline” cardiovascular measures tend to drift upwards across repeated challenge tasks. Basically, Kamarck et al. (1992) endorses computing reactivity change scores using an aggregated baseline measure. However, in the study there were three challenge tasks, each lasting for approximately 6-10 minutes with a minimal resting period (< 5 min) between each task (Kamarck et al., 1992). Therefore, the challenge period was quite long and the recovery time was short. In the present study, a longer recovery period of 10 minutes was used between mental challenge and cold pressor, and a > 10 minute rest between cold pressor and exercise challenge was used. Because the recovery periods in the present study are longer than in the Kamarck et al. (1992) protocol, baseline drift was not expected to be a problem in the present investigation.

Manuck et al. (1989) provides evidence in support of a residual change score approach. The residualized change score provides a means of quantifying the physiologic responses to challenge tasks, while separating the influence of baseline levels from these responses. Although, there are occasions in which the residualized change score differs from the basic change score, these occasions are rare (Manuck et al., 1989). Also, the reliability of both residualized

change scores and basic change scores are comparable (Kamarck et al., 1992). Furthermore, the residual change score approach requires a linear relationship between baseline and task levels, which is not necessarily a valid assumption.

Therefore, arithmetic change scores from baseline to peak levels during the Stroop and cold pressor were used in this study because this method is directly based on the raw data and it is comparable in reliability and outcome to the other two methods (Kamarck et al., 1992; Manuck et al., 1989).

5. Activity Level During Exercise Withdrawal Phase

For the duration of the study (14 days), participants wore an Actiwatch (Mini Mitter Co., Inc, Bend, OR). An Actiwatch is the size and weight of an ordinary wristwatch and is used to measure activity level by a free-moving electrical transducer (piezo-electrode) that detects movement changes in more than one direction. Signals are stored digitally and downloaded on computer for off-line analyses. This device has been validated to differentiate levels of activity (Patterson et al., 1993; Gabbay et al., 1996). Actigraphy was used to document the extent to which participants adhered to the exercise withdrawal instructions, and to objectify the amount of exercise performed by all study participants (Berlin et al., 2003; Kop et al., 2002a).

Sample Size and Power Calculations

Previous findings were used to estimate effect sizes for the current

investigation. The sample size of 40 participants was sufficient to examine all hypotheses at a power >80% ($\beta < 0.20$) with a Type I error (α) set at <0.05 (two-tailed). No adjustments in the α level were made to correct for multiple statistical tests, which is a potential limitation of the present study. All power analyses were performed with the nQuery Advisory power calculation software package.

Statistical analyses to examine the association between the withdrawal of exercise and the effects on psychological and physiological factors were based on 2x3 mixed model analyses of variance (ANOVAs) in which the experimentally induced exercise withdrawn group was compared to the group that continued exercise (2-level between subjects factor) and assessments made over the three study visits were examined as a 3-level within subjects factor. Significant main and interaction effects were further examined using independent and paired t-tests as appropriate.

Power analyses were based on prior research (Chan et al., 1988; Conboy, 1994; Mondin et al., 1996), indicating that the estimated differences between the two groups was one standard deviation (Table 2). The previous work focused on the outcome variable of POMS TMD, therefore the power analyses were based on this dependent variable. It was assumed that the other dependent variables would closely approximate the effect size of the POMS TMD. Power analyses were based on the proposed post hoc between subjects t-tests for group differences. Using the procedures of power estimation described by Cohen (Cohen, 1988), this effect size required 34 subjects (17 per group) to detect between-group differences with $p=0.05$ and a power of 0.80.

To determine if the somatic symptoms of negative affect predicted the development of subsequent cognitive-affective symptoms of negative affect, hierarchical regression analysis was performed. Power for the regression analyses was based on detection of a 10% increase in explained variance by adding one predictor variable (somatic symptoms at visit 2) to a model that already included 4 predictor covariates (somatic symptoms at visit 1, cognitive-affective symptoms at visits 1 and 2, and group allocation) as predictors of cognitive-affective symptoms at visit 3. It was assumed that the 4 covariates would explain approximately 44% variance (equivalent of one standard deviation, i.e., a large effect size) of the dependent variable. Thirty-nine subjects were required to analyze the 10% increase in explained variance of cognitive-affective symptoms by preceding somatic symptoms at a power of 80%.

Table 2: POMS Scores Before and After 2 Weeks Exercise Withdrawal

	Baseline Mean	Baseline SD	Outcome Mean	Outcome SD	p
Mondin et al. (1996)	110.6	26.6	145.3	33.3	<0.05

RESULTS

Sample Characteristics

Participant characteristics are shown in Table 3. The sample was 55% female (a mean age of 31.3 ± 7.5 years, 67.5% Caucasian, 20% Black, 10% Asian, and 2.5% Hispanic).

Table 3. Baseline Sample Characteristics

	Control	Experimental
Total N	20	20
Female	11 (55%)	11 (55%)
Age years (SD)	32.6 (7.8)	30.0 (7.2)
Caucasian	14 (70%)	13 (65%)
Hispanic	1 (5%)	0 (0%)
Asian	2 (10%)	2 (10%)
Black	3 (15%)	5 (25%)
BMI kg/m ² (mean $\pm$ sd)	23.6 $\pm$ 2.9	23.6 $\pm$ 3.2
METS/Week (mean $\pm$ sd)	60.3 $\pm$ 32.8	53.6 $\pm$ 25.9
VO ₂ max mL/kg/min (mean $\pm$ sd)	37.4 $\pm$ 7.9	41.3 $\pm$ 9.5

Manipulation Check

To establish whether the experimental group was adherent to the exercise withdrawal protocol, actigraph data was examined for peak and average activity

levels during exercise withdrawal (Appendix C contains examples of two actigrams; one of a participant in the exercise withdrawal group and one of a participant in the control condition). Based on prior observations (Berlin et al., 2003; Kop et al., 2002a), a

difference in peak activity was expected (means of peak levels across the 14 days) whereas no difference in daily average activity was anticipated. As shown in

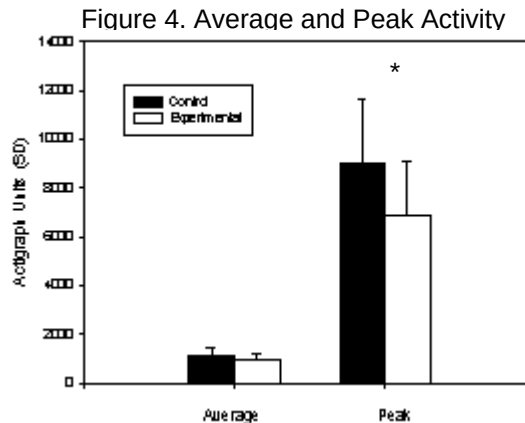


Figure 4, the control group

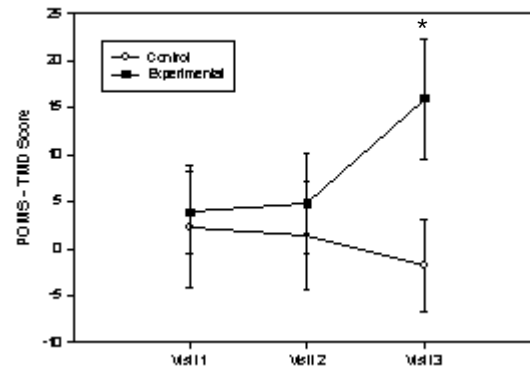
engaged in significantly higher peak activity levels as compared to the experimental group (peak across two weeks: $18,300.0 \pm 6,213.7$ vs. $12,793.8 \pm 7,777.7$; $t(36)=2.4111$; $p=0.021$ and average of peaks: $8,987.4 \pm 2,636.5$ vs. $6,908.9 \pm 2,174.2$; $t(36)=2.65$; $p=0.01$), confirming adherence to the withdrawal procedure. Consistent with prior studies, no statistically significant differences were observed between the control and experimental group on average daily activity levels, but a trend toward this effect was observed ($1,138.4 \pm 284.8$ vs. 975.6 ± 249.1 ; $t(36)=1.88$; $p=0.07$).

Hypothesis 1: Analysis of Changes in Negative and Positive Mood

The four measures of mood assessed in this study were the POMS, BDI, PANAS, and MIVE. Analysis of the POMS revealed that exercise withdrawal induced increased negative mood. A significant interaction between group status

and time ($F_{\text{interaction}}(2,68)=6.07$; $p=0.004$), indicating that as the exercise withdrawal continued, the experimental group developed higher POMS TMD scores as compared to the control group (Figure 5). There were no significant main effects for time ($F_{\text{time}}(2,68)=0.93$; $p=0.40$) or group condition ($F_{\text{condition}}(1,34)=2.14$; $p=0.15$). The post-hoc analyses of the interaction term revealed

Figure 5. POMS TMD Score Across Visits



statistically significant higher negative mood in participants in the exercise withdrawal versus control groups at visit 3 ($t_{\text{visit 3}}(36)=-2.21$; $p=0.03$), where as the groups did not significantly differ at baseline visit 1 ($p=0.84$) and at visit 2 ($p=0.67$).

The same pattern of results was found when examining the BDI scores, revealing a statistically significant interaction between group condition and changes in BDI during exercise withdrawal ($F_{\text{interaction}}(2,68)=7.48$; $p=0.001$).

Figure 6. BDI Score Across Visits

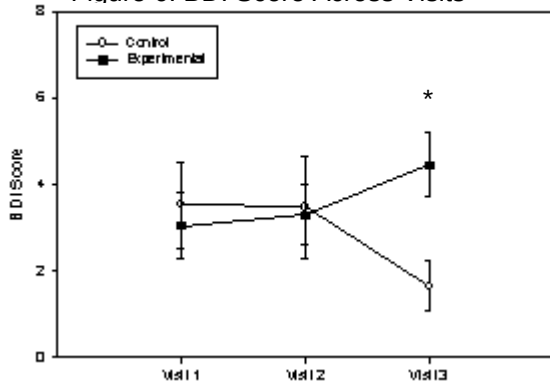
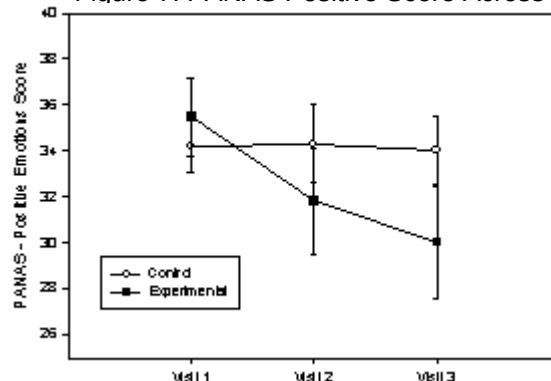


Figure 7. PANAS Positive Score Across



There were no significant main effects for time ($F_{\text{time}}(2,68)=0.16$; $p=0.85$) and group condition ($F_{\text{condition}}(1,34)=1.14$; $p=0.30$). The experimental group showed higher BDI scores compared to controls as the visits progressed (Figure 6), which was significant at visit 3 ($t_{\text{visit 3}}(36)=-3.00$; $p=0.01$). Both the BDI and POMS TMD measure the negative side of mood.

The PANAS was included because this scale assesses both the positive and negative aspects of mood. Consistent with the above-mentioned results regarding negative mood based on the POMS and BDI, a significant interaction ($F_{\text{interaction}}(2,72)=4.17$; $p=0.019$) was observed for the positive emotions. In addition, a significant main effect of time ($F_{\text{time}}(2,72)=4.02$; $p=0.02$) was found, but not for group condition ($F_{\text{condition}}(1,36)=0.94$; $p=0.34$). The experimental group showed a decrease in positive emotions over time compared to the control group which showed little change as the visits proceeded (Figure 7). There were no significant group differences in positive mood at any of the visits ($t_{\text{visit 1}}(36)=-0.63$; $p=0.53$; $t_{\text{visit 2}}(36)=0.86$; $p=0.40$; $t_{\text{visit 3}}(36)=1.35$; $p=0.18$) (Figure 7). The PANAS negative emotion scale did not reveal significant interaction ($F_{\text{interaction}}(2,72)=0.869$; $p=0.424$) or main effects ($F_{\text{time}}(2,72)=3.03$; $p=0.06$; $F_{\text{condition}}(1,36)=0.02$; $p=0.89$) in response to exercise withdrawal.

Hypothesis 2: Somatic Symptoms of Depression Precede and Predict Cognitive-Affective Symptoms

Based on analysis of the somatic and cognitive-affective components of the BDI, a significant interaction was observed between group condition and

change in somatic and cognitive-affective symptoms over time

($F_{\text{interaction}}(2,68)=11.23$; $p=0.001$ and $F_{\text{interaction}}(2,70)=4.49$; $p=0.015$, respectively)

(see Figures 8 and 9). For both types of depressive symptoms, no main effects

of time (($F(2,68)=0.13$; $p=0.88$ and ($F(2,70)=0.02$; $p=0.98$, respectively) or

condition ($F(1,34)=2.81$; $p=0.10$ and $F(1,35)=0.28$; $p=0.60$) were found. No main

Figure 8. BDI – Somatic Scale Score Across Visits

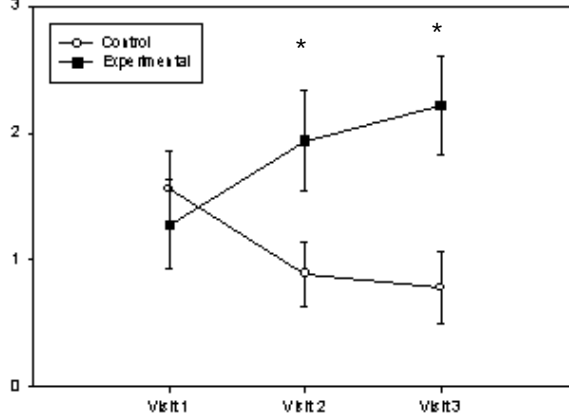
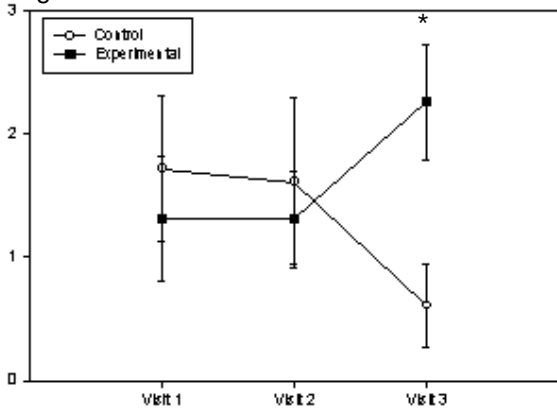


Figure 9. BDI – Affective Scale Score Across Visits



effects of time ($F_{\text{time}}(2,68)=0.13$; $p=0.88$) and group condition

($F_{\text{condition}}(1,34)=2.81$; $p=0.10$) for somatic symptoms and for cognitive-affective

symptoms ($F_{\text{time}}(2,70)=0.02$; $p=0.98$; $F_{\text{condition}}(1,35)=0.28$; $p=0.60$) were found.

Groups differed significantly in somatic symptoms at visits 2 and 3 ($t_{\text{visit } 2}(36)=-$

2.25; $p=0.05$; $t_{\text{visit } 3}(36)=-2.62$; $p=0.01$), whereas cognitive-affective symptoms

were elevated in the exercise withdrawal group at visit 3 only ($t_{\text{visit } 3}(36)=-2.51$;

$p=0.02$) but not during visit 2 ($t_{\text{visit } 2}(36)=0.78$; $p=0.44$). These findings suggest

that somatic symptom changes occurred earlier following exercise withdrawal

(after 1 week) than cognitive affective symptoms (after 2 weeks).

Exhaustion as assessed by the MIVE demonstrated a statistically significantly different change over time when comparing participants in the

exercise withdrawal group versus controls ($F_{\text{interaction}}(2,76)=4.96$; $p<0.01$). Also a significant effect of group condition ($F_{\text{condition}}(1,38)=3.96$; $p=0.05$), reflecting elevated exhaustion levels in the exercise withdrawal condition. The main effect of time was not significant ($F_{\text{time}}(2,76)=0.76$; $p=0.47$). Decomposition of the interaction term into simple effects indicated that the groups differed significantly at visit 3 (MIVE scores 1.25 ± 1.74 vs. 4.05 ± 3.59 in the control and experimental group, respectively; $t_{\text{visit 3}}(36)=-3.14$; $p=0.01$). Exhaustion levels in the exercise-withdrawal group tended to be elevated visit 2 (MIVE scores 1.45 ± 1.90 vs. 2.80 ± 2.73 ; $t_{\text{visit 2}}(36)=-1.81$; $p=0.08$), but not at baseline (MIVE scores 2.25 ± 3.34 vs. 2.25 ± 2.58 ; $t_{\text{visit 3}}(38)=0.01$; $p=0.99$).

In order to evaluate the progression of depressive symptoms, hierarchical regression analysis was performed examining the assessments of somatic and affective symptoms at each of the study visits during the study. The regression model regressed cognitive-affective symptoms at visit 3 (the dependent variable) on somatic symptoms at visit 2 (the primary predictor variable). To control for possible confounding variables, four covariates (group condition, baseline somatic symptoms, baseline cognitive-affective symptoms, and cognitive-affective symptoms at visit 2) were included in the model first, prior to the inclusion of somatic symptoms at visit 2. After adjusting for the aforementioned control variables, the somatic symptoms at visit 2 were predictive of cognitive-affective symptoms at visit 3 (R^2 change=0.088; $\beta=0.618$; $p=0.046$) (see Table 4). Therefore, in the progression of mood-related symptoms, somatic symptoms are present first and then predict subsequent cognitive-affective symptoms.

Exploratory analyses were conducted to examine whether cognitive-affective symptoms at visit 2 were predictive of subsequent cognitive-affective symptoms at visit 3, which was not supported by the present data (R^2 change=0.001; Beta=-0.088; p =0.621).

We carefully examined the potential of multicollinearity by examining the tolerance and variance inflation factor (VIF) of each of the predictor variables. The VIF is the inverse of tolerance, defined as $(1/(1-R_i^2))$. As the VIF increases, so does the variance of the regression coefficient. Biases resulting from multicollinearity are expected to be unlikely because of the overall moderate intercorrelations between the predictor variables, and the moderate correlation between each independent variable with the dependent variable (Table 4).

Table 4. Predictors of Cognitive-Affective Symptoms of Negative Affect

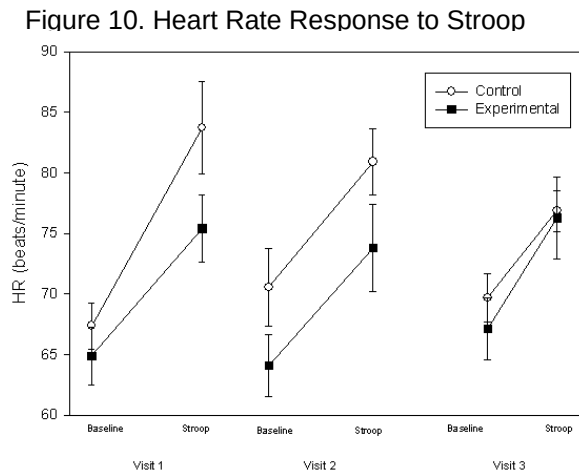
Predictor	B	Standard Error	B	T	ρ	Zero-order r	Partial r	Tolerance	VIF
Condition	1.11	0.68	0.28	1.63	0.11	0.45	0.29	0.69	1.45
Affective-cognitive symptoms at Visit 1	0.20	0.18	0.25	1.14	0.27	0.26	0.20	0.43	2.35
Somatic symptoms at Visit 1	-0.24	0.31	-0.17	-0.79	0.44	0.19	-0.12	0.42	2.40
Affective-cognitive symptoms at Visit 2	-0.09	0.18	-0.11	-0.50	0.62	0.20	-0.09	0.44	2.30
Somatic symptoms at Visit 2	0.62	0.30	0.48	2.10	0.05	0.52	0.36	0.38	2.64

Hypothesis 3: Reactivity to Challenge

It was hypothesized that exercise withdrawal would increase hemodynamic and emotional reactivity. As discussed in the methods section, reactivity was evaluated as arithmetic change scores from baseline to peak level during the challenge tasks (Stroop and cold-pressor). Specifically, task reactivity was defined as the peak hemodynamic response during the task subtracted from an average of three measurements of hemodynamic response during the rest period. A statistically significant interaction was observed between condition and visit on HR reactivity during the Stroop task (Figure 10). The control group showed an attenuation of HR response across the visits, whereas the experimental group's HR did not show an attenuation ($F_{\text{interaction}}(2,72)=3.792$, $p=0.027$). A statistically significant main effect for time ($F_{\text{time}}(2,72)=5.87$; $p=0.004$), but not for group condition ($F_{\text{condition}}(1,36)=0.30$; $p=0.59$). Analyses of simple effects revealed a significant decrease in reactivity over time in the control group from visit 1 to visit 2 ($t_{\text{visit 1-2}}(18)=2.55$; $p=0.02$), and a trend for decrease in reactivity from visit 2 to 3 ($t_{\text{visit 2-3}}(18)=1.75$; $p=0.10$), but not in the experimental group. The significant interaction could be a result of regression to the mean of the initially high HR response in the control group at visit 1 (Figure 10), which is supported by the trend towards higher HR reactivity in the control group as compared to the exercise withdrawal group at baseline ($t_{\text{visit 1}}(36)=1.83$; $p=0.08$), which was not observed during later visits ($t_{\text{visit 2}}(36)=0.24$; $p=0.81$; $t_{\text{visit 3}}(36)=-0.85$; $p=0.40$).

For SBP and DBP reactivity during the Stroop task, no statistically

significant effects of exercise withdrawal were observed (SBP: $F_{\text{interaction}}(2,72)=0.32$; $p=0.71$; DBP: $F_{\text{interaction}}(2,72)=0.46$; $p=0.64$). Blood pressure responses displayed a significant attenuation during the study (SBP: $F_{\text{time}}(2,72)=15.21$; $p=0.001$; DBP: $F_{\text{time}}(2,72)=8.26$; $p=0.001$). Further analyses revealed that the attenuation of blood pressure responses to mental challenge occurred from visit 1 to visit 2 ($p's \leq 0.04$) as well as from visit 2 to visit 3 ($p's \leq 0.02$). No main effects for group condition were observed (SBP: $F_{\text{condition}}(1,36)=0.002$; $p=0.96$; DBP: $F_{\text{condition}}(1,36)=0.11$; $p=0.74$).



Regarding reactivity to the cold pressor, effects of exercise withdrawal were not significant with respect to hemodynamic reactivity (HR: $F_{\text{interaction}}(2,56)=.06$; $p=0.35$; SBP: $F_{\text{interaction}}(2,56)=0.66$; $p=0.52$; DBP: $F_{\text{interaction}}(2,56)=1.24$; $p=0.30$). Also, no statistically significant main effects of time (HR: $F_{\text{time}}(2,56)=0.15$; $p=0.86$; SBP: $F_{\text{time}}(2,56)=0.05$; $p=0.95$; DBP: $F_{\text{time}}(2,56)=0.18$; $p=0.83$) or group condition (HR: $F_{\text{condition}}(1,28)=0.04$; $p=0.84$; SBP: $F_{\text{condition}}(1,28)=0.29$; $p=0.60$; DBP: $F_{\text{condition}}(1,28)=1.08$; $p=0.31$).

Exercise withdrawal had various effects on emotional reactivity to challenge. The experimental group displayed a different change in positive emotions (amusement and happiness) to the Stroop task during the course of the study compared to the control group ($F_{\text{interaction}}(2,72)=5.37$; $p=0.007$). No main effects for time ($F_{\text{time}}(2,72)=1.25$; $p=0.29$) or group condition ($F_{\text{condition}}(1,36)=0.02$; $p=0.88$) were observed. Examination of simple effects suggests that the significant condition x visit interaction term most likely reflected group differences at baseline (0.58 ± 1.40 vs. -0.21 ± 1.03 ; $t_{\text{visit 1}}(38)=1.85$; $p=0.07$) with the control group showing higher positive emotions during the Stroop task compared to the experimental group, and not during the course of exercise withdrawal ($t_{\text{visit 2}}(36)=0.60$; $p=0.95$; $t_{\text{visit 3}}(38)=0.56$; $p=0.58$) where the two groups showed similar positive emotional reactivity to the Stroop task.

For the negative emotion reactivity (anger, frustration, irritation, anxiousness, and stressfulness) to the Stroop, a trend for the experimental group to display more negative emotional reactivity to the Stroop as the visits progressed was found, although this effect did not reach statistical significance ($F_{\text{interaction}}(2,72)=2.79$; $p=0.07$). No main effects of time ($F_{\text{time}}(2,56)=0.05$; $p=0.95$) or group condition ($F_{\text{condition}}(1,28)=0.29$; $p=0.60$) on emotional reactivity to the Stroop were observed.

During the cold pressor, emotional reactivity (positive and negative emotions) did not change in response to exercise withdrawal and there were no main effects of time or group condition (Positive: $F_{\text{interaction}}(2,70)=2.01$; $p=0.14$; $F_{\text{time}}(2,70)=0.08$; $p=0.93$; $F_{\text{condition}}(1,35)=0.87$; $p=0.36$; Negative:

$F_{\text{interaction}}(2,70)=0.26$; $p=0.77$; $F_{\text{time}}(2,70)=2.18$; $p=0.12$; $F_{\text{condition}}(1,35)=0.43$; $p=0.52$).

Hypothesis 4: Fitness Changes

Fitness levels were examined for visit 1 and visit 3 only. Participants also completed a low-level exercise test at visit 2, but the procedures for the exercise test at visit 2 were not comparable to the other two exercise tests as a result of different work loads (70% versus 85% of maximal age-adjusted heart rate). At visit 2, the test was stopped at 70% of age-predicted maximum heart rate to ensure the exercise-withdrawn participants did not receive a cardiovascular workout during visit 2, which would have compromised the two-week exercise withdrawal period (see Discussion section for further consideration of this issue).

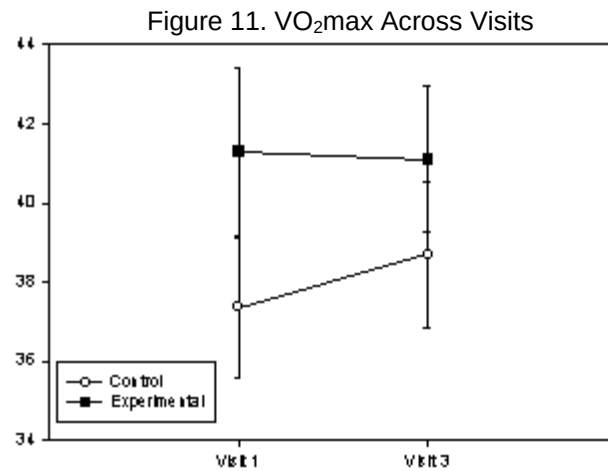
At baseline, the control and experimental groups were comparable on fitness measures (Tables 3 and 5). As shown in Table 5, 32% of the participants in the exercise withdrawal group completed fewer stages than at study entry, which is significantly more than observed in the control group (5%; $p=0.031$). None of the other fitness markers showed statistically significant group differences (Table 5). The primary variable used to assess fitness level for further analyses was $VO_2\text{max}$ (see Methods) (Mitchell et al., 1958).

It was hypothesized that an interaction between group condition and visit would occur, such that the exercise withdrawal group would show a decrease in $VO_2\text{max}$ across the study, whereas the control group would not show such a

decrease. The control group tended to display increases in VO_2max over time ($p=0.05$), whereas the exercise withdrawal group displayed no change in fitness levels ($p=0.59$) (Figure 11). Despite the trend, the interaction term did not reach statistical significance ($F_{\text{interaction}(1,36)}=2.71$; $p=0.11$). Also, there were no main effects of time ($F_{\text{time}(1,36)}=1.30$; $p=0.28$) or group condition ($F_{\text{condition}(1,36)}=1.88$; $p=0.18$).

Table 5. Measures of Fitness During 2 Weeks Exercise Withdrawal (EW)

	Control		Experimental	
	Pre EW	2 Weeks No EW	Pre EW	2 Weeks EW
VO_2max (mL/kg/min)	37.4 (7.9)	38.7 (8.2)	41.3 (9.5)	41.1 (9.0)
Stage 1 HR (beats/min)	103.3 (11.1)	102.1 (9.3)	99.1 (13.4)	95.6 (14.2)
Total Exercise Time (min)	10.5 (2.0)	10.8 (2.0)	11.3 (2.1)	11.1 (2.3)
# of Stages Completed	3.3 (1.0)	3.4 (1.0)	3.7 (1.1)	3.5 (1.8)
Peak Watts	142.5 (30.6)	145.5 (31.2)	153.0 (37.6)	153.2 (42.3)
Peak HR	160.1 (10.5)	158.9 (7.6)	158.5 (11.2)	156.7 (10.2)
Peak Tidal Volume	1.4 (0.5)	1.5 (0.5)	1.6 (0.5)	1.6 (0.5)
Peak Breathing Frequency	34.6 (8.4)	34.9 (7.6)	36.1 (7.5)	35.9 (5.1)
Peak Minute Ventilation	47.3 (18.8)	50.2 (15.8)	55.9 (18.7)	56.1 (13.6)
Recovery HR 2 minutes post	130.8 (14.4)	126.4 (12.0)	123.5 (13.6)	122.3 (12.3)
Borg Scale	13.5 (2.0)	14.2 (2.0)	14.9 (2.0)	15.6 (2.2)
Drop in Stages Completed	-----	5%	-----	32%

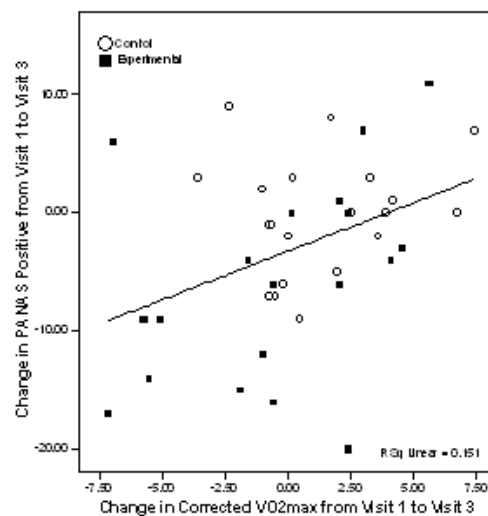


The changes in fitness were not correlated with protocol compliance as measured by the average of daily peak values in activity, but showed a trend in the hypothesized direction ($r=0.280$; $p=0.094$). As the daily peak values decreased, the fitness level decreased.

Hypothesis 5: Changes in Fitness Relationship to Symptoms and Reactivity

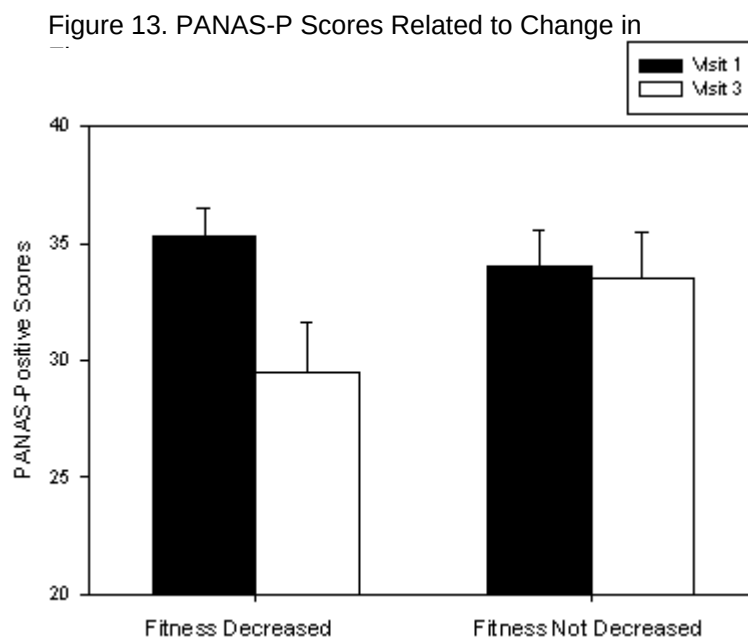
Changes in fitness level tended to be associated with changes in negative

Figure 12. Relationship between Change in Fitness and Change in PANAS-P



mood as assessed by the POMS TMD score ($r=-0.287$; $p=0.085$). As the fitness level decreased, the POMS TMD increased (an increase in negative mood). The changes in fitness were correlated with the changes in PANAS-P ($r=0.389$; $p=0.014$) across visits 1 to 3 (Figure 12), indicating that decreased fitness levels were associated with decreased positive mood. The changes in fitness were not statistically significantly correlated with the changes in mood as measured by the other questionnaires (r 's $=-0.033-0.112$; p 's >0.5).

Because exercise withdrawal resulted in a significant ($p=0.031$) number of participants who dropped in the number of completed stages at visit 3, the sample was divided into participants who displayed decreased fitness ($n=17$) versus those who did not decrease fitness ($n=19$). As shown in Figure 13, participants with a decreased fitness level during the protocol displayed a decrease in positive mood (PANAS-P: $F_{\text{interaction}}(1,37)=5.412$; $p=0.03$). A



significant main effect for time, with an overall decrease in PANAS-P scores ($F_{\text{time}}(1,37)=7.53$; $p=0.009$) was found. The main effect for group condition was non-significant ($F_{\text{condition}}(1,37)=0.38$; $p=0.54$), and group differences in positive mood were non-significant at both visit 1 and visit 3 ($t_{\text{visit 1}}(37)=-0.63$; $p=0.54$; $t_{\text{visit 1}}(37)=1.38$; $p=0.18$). A similar trend for increased negative mood (POMS TMD) among participants with reduced fitness was observed ($F_{\text{interaction}}(1,35)=3.97$; $p=0.054$), whereas main effects for time and group were non-significant ($F_{\text{time}}(1,35)=1.06$; $p=0.31$; $F_{\text{condition}}(1,35)=0.93$; $p=0.34$).

In order to examine whether the predictive value of fitness changes on mood did not reflect differences at baseline and group condition, multiple regression analyses were conducted, adjusting for baseline fitness level and group condition (control vs. experimental). For the PANAS-P, the predictive value of the change in fitness level was not statistically significant after adjusting for baseline fitness and group status (R^2 change= 0.057; $\beta=0.267$; $p=0.115$). For the POMS TMD, the same pattern of results was found, with a statistically non-significant result for the predictive value of the change in fitness level on the change in POMS TMD after adjusting for baseline fitness and group status (R^2 change=0.015; $\beta=-0.132$; $p=0.421$).

Changes in fitness level were not associated with changes in reactivity as measured by hemodynamic reactivity (SBP, DBP, and HR) and emotional reactivity (positive and negative emotions in response to challenge) to both mental and physical challenge (Stroop and cold-pressor). The magnitude of the relationships were small (r 's=-0.04-0.19; p 's>0.40) and there was not a distinct

pattern in the results suggesting increased or decreased reactivity in response to changes in fitness.

DISCUSSION

This investigation examined the effect of exercise withdrawal on mood and on fitness. Mood changes following 2 weeks of exercise withdrawal included fatigue, depressive symptoms, and a reduction in positive affect. A novel finding of the present study was the order in which depressive symptoms developed. Specifically, the development of somatic symptoms, particularly fatigue, preceded and predicted the development of cognitive-affective symptoms (sadness and feelings of guilt). In addition, individuals developing reduction in fitness following exercise withdrawal may be more prone to subsequent mood changes.

Analysis of Mood Changes

The present observations are consistent with prior research (Conboy, 1994; Morris et al., 1990; Szabo, 1995), demonstrating that exercise withdrawal increased depressive symptoms (BDI), increased fatigue (MIVE), decreased positive emotions (PANAS-P), and increased negative mood (POMS TMD). A statistically significant difference on negative emotions as measured by the PANAS-N was not found. The PANAS-N only has 10 items whereas the POMS TMD has 67 items. Both scales address symptoms over the course of a week and are based on 5-point Likert scales. However, the POMS TMD is a more thorough examination of the various components of negative mood. The PANAS-N is a less precise assessment of negative mood because of the minimal

number of items. “Scared” and “hostile” are both included on the negative scale of the PANAS, but may not be as relevant to the negative emotions induced by exercise withdrawal as “sluggish” and “weary” which are included on the POMS TMD. Therefore, the specific item content of negative emotions as measured by the PANAS-N may not be as relevant as the POMS TMD to the effects of exercise withdrawal. In prior research on exercise withdrawal, the POMS has been used almost exclusively (Conboy, 1994) providing a good measure of negative mood, but a measure of positive mood should also be included in future studies (Szabo, 1995).

By employing different types of mood assessments, components of mood (somatic vs. affective) and their time trajectory during exercise withdrawal were examined. The BDI consists of two primary components (Whisman et al., 2000): somatic symptoms and cognitive-affective symptoms. This investigation documented that the mood disturbances caused by exercise withdrawal involve somatic symptoms first, followed by cognitive-affective symptoms. Morris et al. (1990) reported that the development of somatic symptoms preceded the development of cognitive-affective symptoms in an exercise withdrawal paradigm, but the predictive ability of somatic symptoms was not investigated. In the present study, somatic symptoms occurred first and predicted subsequent development of cognitive-affective symptoms. It is noteworthy that in contrast to the predictive value of somatic symptoms following one week of exercise withdrawal, no parallel predictive value was found for cognitive-affective symptoms assessed at the same time. The development of depressive

symptoms (predictive ability of somatic symptoms) may be of value in the determination of people at risk for developing full depressive episodes in response to the lack of exercise, which is more common in an injury population (although still largely undiagnosed).

Reactivity to Challenge

The observed hemodynamic and emotional responses to challenge were dependent on the type of challenge tasks (mental vs. physical). In response to the Stroop challenge task, a lack of attenuation of HR response was found in the exercise-withdrawn participants. However, the statistically significant effect could have been a result of the relatively high response magnitude in the control group at baseline. Therefore, the examination of the components driving the initially elevated HR response will be important. HR is controlled by both the sympathetic and parasympathetic nervous systems. Heart rate variability (HRV) is a marker of parasympathetic activity and is increased by fitness (Bryan, Ward, & Rippe, 1992; Smith, Hudson, Graitzer, & Raven, 1989). In order to clarify the HR finding, to determine if it is a lack of attenuation or a high responsive control group, the examination of parasympathetic activity via HRV will be important to further explore. The present study obtained assessments of heart rate variability, but this thesis primarily addresses fitness (assessed by $VO_2\text{max}$) as the physiological parameter of interest, hence results related to heart rate variability are beyond the scope of this thesis.

The reactivity to the cold-pressor challenge task did not reveal significant changes caused by exercise withdrawal in BP or HR, and did not attenuate in either the control or experimental group. Therefore, it is possible exercise withdrawal does not affect the response to challenge per se, but rather the attenuation to a repeated stressor. The lack of exercise may cause a lack of the normal attenuation response to a repeated stressor. The reason the cold-pressor may have elicited no differences between the groups is because it is not subject to attenuation. Also, the cold-pressor measures a response to cold and pain (Patterson et al., 1995) and these particular responses may not vary with exercise withdrawal, as it is partly a physical stressor (cold) (Lovallo, 1975). Another possibility is the mood changes caused by exercise withdrawal are more relevant to a mental challenge than a physical challenge.

We also conducted exploratory analyses examining the relationship between the two domains of psychological parameters: mood symptoms and hemodynamic and mood reactivity. Most studies do not reveal strong associations between negative mood or depression with hemodynamic reactivity. A few studies have demonstrated reduced reactivity among individuals with distress, Post-Traumatic Stress Disorder (PTSD), and exhaustion (Casada, Amdur, Larsen, & Liberzon, 1998; Orr & Roth, 2000; van Doornen & van Blokland, 1989). In the present study, the visit 2 symptoms were highly correlated with visit 2 hemodynamic responses to the Stroop challenge, especially the somatic components of depression (r 's range from -0.434 to -0.610; p 's < 0.05). These results support the findings of reduced response to

challenge in depressive patients. However, the relationship between symptoms at visit 3 and hemodynamic reactivity was not statistically significant. Therefore, it is possible that the somatic symptoms of depression (such as fatigue) are related to reactivity to a challenge (i.e., somatic symptoms relationship to SBP at visit 2: $r=-0.33$; $p=0.04$), whereas once cognitive-affective symptoms develop the relationships diminishes (e.g., at visit 3, cognitive-affective symptoms relationship to SBP: $r=-0.01$; $p=0.95$; somatic symptoms relationship to SBP at visit 3: $r=-0.08$; $p=0.61$). The somatic symptoms (fatigue) may be more relevant to reactivity to challenge than the cognitive-affective symptoms in the setting of exercise withdrawal (feeling blue). It is conceivable that the initial fatigue may cause a decrease in reactivity resulting from a lack of engagement in the challenge activity, but further studies are needed to reveal the transient nature of this phenomenon.

Fitness Changes

As mentioned in the Results section, the visit 2 exercise test was not analyzed in comparison to the visits 1 and 3 exercise tests as a consequence of the differences in protocol. At visits 1 and 3, the exercise test proceeded until 85% of age-predicted maximum heart rate. But at visit 2, the test was stopped at 70% of age-predicted maximum heart rate to ensure the exercise-withdrawn participants did not receive a cardiovascular work-out during visit 2, which would have compromised the two-week exercise withdrawal period. However, by

changing the exercise procedure at visit 2, the comparison between visit 1 and 3 performance with visit 2 performance becomes difficult to interpret. First, the participants knew that the exercise test would be shorter at visit 2 and this expectation of lower exertion can change anticipatory heart rate response to exercise (Stamps, 1986). There was a trend in the present study for HR at the end of the warm-up stage to be lower at visit 2 than at visit 1 ($F(1,36)=3.07$; $p=0.09$; 101.2 ± 12.4 beats/min vs. 99.7 ± 13.6 beats/min), which supports a change in anticipatory heart rate with the expectation of lower exertion.

In addition to potential confounding resulting from anticipatory heart rates, estimations of $VO_2\text{max}$ from a submaximal procedure are sensitive to the level of heart rate reached. A higher percentage of age-predicted maximum heart rate obtained leads to a more accurate prediction of $VO_2\text{max}$ (Storer, Davis, & Caiozzo, 1990). Therefore, different predictive values would be obtained from the visit 2 data. Comparing peak values on the exercise tests would not be analogous because the peak at the visit 2 exercise test would be at a lower workload than the visit 1 and 3 peak values. A comparison of $VO_2\text{max}$ at 70% of age-predicted maximum heart rate is also not possible because HR measurements are obtained at the end of stages to ensure a plateau in HR has been achieved at each workload. At visits 1 and 3, 70% of age-predicted maximum heart rate most likely does not occur at the end of a stage. Therefore, the HR data for 70% at visits 1 and 3 is unavailable based on the present data.

The fitness level of exercise-withdrawn participants was not statistically significantly different from the control participants. However, in examining the

number of stages completed during the exercise test, the exercise-withdrawn group completed less stages at visit 3 as compared to visit 1. However, there was not an overall interaction effect in number of stages completed, with the exercise-withdrawn participants showing a decrease in the number of stages completed and the control group remaining relatively stable in stages completed. In the exercise-withdrawn group, a subgroup of participants (n=7) completed fewer stages. The effect of exercise withdrawal evidenced by this subgroup was not strong enough for an interaction effect to be statistically significant. The power to detect an interaction effect is lower than the power to detect a within-subjects effect. The difference in the power to detect an effect between the two analyses is a possible explanation for the disparate results. A post-hoc power analysis revealed that the power to detect the interaction effect was only 0.38.

For the fitness variables (i.e., minute ventilation, VO_2max) there was a trend (not statistically significant) in the predicted direction, suggesting that the exercise-withdrawn group had lower fitness levels than the control group as the study visits progressed. For peak performance during the exercise test, peak HR was not hypothesized to change because the HR was used to determine the end of the exercise test. Therefore, it was in the protocol that all participants would reach 85% of age-predicted maximum heart rate at both visit 1 and 3.

There are several possible reasons for the lack of statistical significance in the fitness variables. First, the power analyses for this study were directed at the detection of mood changes. There were no previous studies involving exercise withdrawal and fitness changes over a two-week withdrawal period to base a

power analysis. The only previous study exploring the effect of exercise withdrawal on fitness was for one week and there was not a decrease, but an increase in VO_2max (not to statistically significant degree) (Szabo et al., 1992). Thus, the present study may have been underpowered to detect a fitness change. A second possibility is that the measures used were too insensitive to detect the subtle changes in fitness that occurred. Finally, the two-week withdrawal period may have been too short to induce substantial fitness changes.

Changes in Fitness as Related to Symptoms

Although overall fitness did not change, the relationship between the changes in fitness was correlated with the changes in symptoms across the two-week period. Both a decrease in positive emotions (PANAS-P) and an increase in negative emotions (POMS TMD) were correlated with changes in fitness. Dichotomizing groups into individuals developing reduced fitness versus those without decreases in fitness compared to baseline fitness level at study onset, revealed the same pattern of results. However, when these analyses were adjusted for baseline fitness level and group condition (control vs. exercise withdrawal), the statistical significance disappeared. Therefore, it is possible the effects of fitness are not robust in the exercise withdrawal paradigm or fitness change is a minor factor in the psychological changes associated with exercise withdrawal.

Limitations

The present observations may not be generalizable to the biobehavioral processes characteristic of sedentary individuals because this investigation enrolled individuals with normal weight who were physically fit. The mechanisms explaining reactions to lack of exercise may not be the same mechanisms that explain a prolonged sedentary lifestyle. The consequences of a sedentary lifestyle can take years to develop and are multifactorially determined; therefore a two-week manipulation of physical activity may not mirror the various complications of a sedentary lifestyle. The paradigm used in the present study is potentially more relevant to the mood changes observed in response to involuntary withdrawal of exercise, such as observed in response to injuries. Further studies are needed to establish comparability of the present observations and those that occur in sports and other injuries.

Another limitation of the present investigation was that potential participants were excluded if they were over the age of 45. The limited age range used in the study limits the generalizability of the results to an older population. Prior research on the relationship between exercise and age has documented physiological differences in the reaction to exercise between older and younger populations. For example, muscle metabolic capacity (a contributor to VO_2max), which is increased by engaging in exercise, shows a smaller increase in older compared to younger people (Hunter et al., 2002). However, in the relationship between exercise and mood changes, age has not been found to be a moderator (Rocheleau, Webster, Bryan, & Frazier, 2004). Therefore, the

results involving mood changes are more likely to be generalizable to an older population than the physiological changes observed. If an older population had participated in the study, more dramatic physiological changes might have been observed due to a decrease in exercise tolerance with aging (Skaluba & Litwin, 2004).

Participants were not blind to the experimental manipulation. This study characteristic may have affected the observed trajectories in symptomatology and also affected baseline characteristics (e.g., elevated heart rate responses to the Stroop task and decreased positive mood during that task). It would not be difficult for the participants to discern the hypotheses concerning mood changes associated with lack of exercise. Nonetheless, the observed physiological changes were consistent with the study hypotheses, although not reaching traditional ($p=0.05$) cut-offs for statistical significance. The observed pattern in fitness results adds validity to the success of the experimental manipulation of this investigation. In other words, the participants may have been aware of the mood hypotheses and answered the questionnaires according to expectation, but the observed changes in fitness may be less subject to the participants' expectations. Also, the participants who developed a decrease in fitness were the ones who also experienced decreases in mood; therefore, the participants' expectation and lack of blindness to the conditions were possibly minor contributors to the outcomes.

The comparison used in the study was a comparison of lack of exercise to continuation of exercise. However, the manipulation involved deprivation of an

activity (exercise). The results of the study could reflect consequences of being deprived of an activity, rather than specifically being deprived of exercise. Therefore, the effects of deprivation from exercise versus deprivation from an activity in general were not explored in this study.

No adjustments in the α level were made to correct for multiple statistical tests, which is a potential limitation of the present study. Although, the α level of each test was set at $\alpha < 0.05$, the Type I family wise error rate was higher than this value. A Fisherian approach was used in the statistical analyses of this thesis, whereby only omnibus statistically significant tests were examined further with additional post-hoc tests. However, another approach that could have been employed would have been to adjust the α level for the number of tests to be performed (Bonferroni correction). The analyses may have been subject to an increased Type I error rate (increased chance of finding false positive results).

Future Directions

Future research may focus on the other pathways by which the lack of exercise can cause mood and reactivity changes. Specifically, autonomic nervous system balance and inflammation factors can be examined in order to determine if these physiological activities are predictive of the mood changes as repeatedly observed in response to exercise withdrawal (see proposed model in Figure 1).

A widely researched factor in the relationship between mood and physical activity concerns the role of endogenous opiates and endorphins. In general, endorphins are known to be involved in pain and pleasure responses in the central nervous system. Experiments have demonstrated that aerobic exercise in various forms cause elevations in β -endorphin levels (Goldfarb & Jamurtas, 1997). The level of athletic training of study participants seems to play a minor role as both trained and untrained individuals experience an increase in β -endorphin levels in response to acute exercise, although metabolism of β -endorphin is more efficient in trained athletes (Goldfarb et al., 1998). Studies have demonstrated that both intensity and duration are factors in increasing β -endorphin concentrations, which means that exercise levels at above 60% maximum oxygen uptake ($VO_2\text{max}$) (Goldfarb et al., 1997) and performing for a minimum of 3 minutes are required to result in a measurable endorphin response. Despite the effects of exercise on β -endorphin levels, β -endorphins are not necessary for the euphoria experienced by exercising. Harte et al. (1995) reported that exercise produced both a positive emotional effect and a rise in the levels of β -endorphin, but they are not highly correlated.

Experiments in which significant amounts of β -endorphin were directly injected into the bloodstream of non-depressed participants failed to show any mood changes. On the other hand, β -endorphin injections had an effect on clinically depressed patients. In future research, β -endorphin and other neurotransmitters may be examined to determine their impact on the psychological consequences of lack of exercise.

Future research comparing voluntary exercise withdrawal with forced exercise withdrawal (i.e., injury) may reveal important information regarding the pattern of symptomatology and physiology in injured individuals. Injured individuals may have inflammatory factors operating that also effect mood parameters. Mood changes following injury may adversely impact medical recommendations related to low-exercise level adherence. In addition, chronic disease populations such as rheumatoid arthritis patients and heart failure patients can also be studied to determine the interactive effects of lack of exercise inherent in the disease and subsequent symptomatology. Future research can focus on clarifying the mechanisms that link psychological factors (i.e., mood and reactivity) with underlying physiology in terms of exercise. The above suggestions for research focus on examining these relationships from different population perspectives.

In future research, the addition of another control group would help correct one of the limitations of this experiment. In the present study, a group of continuing exercisers was compared to a group of exercisers deprived of an enjoyable activity. An appropriate additional control group would also be deprived of an activity to determine if the mood changes were caused by lack of exercise, specifically, or caused by the lack of a routine pleasant activity, in general.

The present study has identified fitness levels as one possible mechanism accounting for the prevalence of negative mood commonly observed in sedentary individuals as well as individuals deprived of usual exercise activities.

The clarification of additional biobehavioral mechanisms may help to further elucidate the relationship between physiology, biology, and mood in terms of fitness and exercise training.

Implications

Despite the limitations of the present investigation, the findings provide important information on the role of fitness in the development of mood changes caused by exercise withdrawal. Previous work in this area has focused on survey and case-control research, which precludes inferences on causality. By examining the relationship in an experimental model, the time trajectory and relationship of both mood symptoms and physiological changes were studied. By providing preliminary information on these outcomes, this study helps to establish the progression of depressive symptoms (somatic first, then cognitive-affective). It emphasized the need for more research utilizing a thorough examination of the time trajectory of fitness changes which use more sensitive measures than those in the present research (such as lactate and oxygen consumption measures). By continuing such work, the consequences of lack of exercise (voluntary and involuntary) can be thoroughly understood. Consequentially, interventions to offset these outcomes can be constructed to lessen the burden felt by those who are exercise-withdrawn. The relatively minor exercise-withdrawal paradigm used in this study did not induce depressive symptoms to a clinical degree. However, investigations of more extreme

exercise-withdrawal (such as injury) may reveal a pronounced, clinical effect on mood. Interventions may be an essential component of the rehabilitation process in these cases of severe exercise withdrawal.

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Appendix A: Informed Consent Document

Research Study Entitled: Physiological and Mood Changes Induced by Exercise Withdrawal

Healthy Volunteers

I. Introduction

You are being asked to take part in a research study. Before you decide to be a part of this study, you need to understand the risks and benefits so that you can make an informed decision. This is known as *informed consent*.

This consent form provides information about the research study. Once you understand the study and the tests it requires, you will be asked to sign this form, if you want to take part in this study. Your decision to take part is **voluntary**. This means you are free to choose if you want to take part in this study.

II. Purpose and Procedures

The Department of Medical and Clinical Psychology of the Uniformed Services University of the Health Sciences (USUHS) is conducting a study to examine the effects of exercise withdrawal on physical function and mood. Regular exercise has beneficial effects on physical and mental health and this project aims to increase our knowledge of how exercise affects physical and mental function. In order to do this, we will compare the effects of voluntary exercise withdrawal with the loss of exercise in participants who have had an injury.

Sixty participants will take part in this project. Twenty will stop exercising, 20 will not stop exercising, and 20 will be asked to participate because they have had a recent injury. We estimate the total testing time to be two hours for each of the three visits (a total of 6 hours). The three visits will take place over a 16-day period. To be eligible for this study, you must be in good physical health, be available for all three visits, and regularly exercise three times per week for more than 30 minutes. If you are a medical or nursing student at USUHS, prior to your participation in the study, you must receive approval from your Commandant.

You cannot participate in the study if you are older than 45 or younger than 18, if you regularly use anti-inflammatory such as aspirin (acetylsalicylic acid) or Tylenol (acetaminophen), if you regularly use anti-coagulant medication, if you have a history of cardiovascular disease, if you have hypertension (blood pressure >140/90 mmHg), if you are obese (BMI > 30 kg/m²), if you are currently under the treatment of a psychiatrist or psychologist for a mental disorder, or if you are a military participant and your scheduled Physical Performance Testing

(PPT) < 1 month away.

You will be asked to continue your regular activities as usual for two days after the first study visit. After those two days, half of the participants will be asked to stop their regular exercise workouts.

III. Overview of the Study

You will be asked to come to the research site three times over a period of 16 days. We will ask you to perform mental and physical performance tasks and complete a set of questionnaires. Your heart rate, blood pressure, and blood clotting factors will be examined at each of the three visits. During the course of this study, we ask you to wear a wristwatch activity monitor.

The details of what you will be asked to do are described below and include: 1) questionnaires; 2) mental performance tasks; 3) physiological measures (heart rate, blood pressure, and lung function); 4) blood draw; 5) physical challenge tests (cold exposure and bicycle exercise); 6) possibly withdrawing of your usual exercise level for 14 days (depending on the group you will be in, please see below).

IV. Study Procedures

1. Questionnaires

You will be asked to complete a set of questionnaires about your health, physical activity and mood. For these questionnaires, we ask that you answer all items to the best of your ability. We will also conduct and tape-record a brief interview to assess your mood at each study visit.

Questionnaires and interviews will be coded with a unique identification number so that you are not personally identified.

2. Mental Performance Tasks

At each visit, you will be asked to watch a 1-minute film clip and perform a 5-minute computer task. The computer task is similar to other computer games. You will be asked to press a mouse button as fast as you can when particular words or colors appear on the screen.

3. Physiological Measures

To assess your heart rate, six pads will be placed on various places on your chest and neck. These pads should present no discomfort. Blood pressures will be collected repeatedly during the mental and physical tasks by a cuff placed on your upper arm. To assess the your heart's pump function, four tape strips will be placed around your stomach and

neck (this is called an “impedance cardiogram”). The tape is used to improve detection of the electrical signal from your heart. Blood pressure and heart function measurements are safe and established clinical techniques used to assess your physiological responses.

4. Blood Drawing

On each study visit one blood sample prior to the exercise test will be collected by a trained technician. The total amount of blood drawn during any one visit will not exceed 20 ml (about two tablespoons). Your blood will be analyzed for inflammation and blood clotting factors.

5. Physical Performance Tasks

You will be asked to perform a cold-immersion test and a bicycle exercise test at each visit. For the cold-immersion task you will be asked to put your hand in a bucket of ice water for 2.5 minutes. If the cold becomes too uncomfortable, you can stop the task earlier than 2.5 minutes. The bicycle test involves sitting on a stationary bicycle and pedaling at 50 rounds per minute at four different workloads for two minutes at each workload. The workloads are below your maximal exercise level and range from very light to moderate. During the exercise test, you will also be asked to breathe into a mouthpiece (spirometer) while wearing a nosepiece to determine your lung function.

6. Exercise Withdrawal

During the study you will be assigned to either stop your current exercising or continue with your usual exercise level (see the introduction above for details). Half of the participants in this study are asked to stop their regular exercise levels, the other half are asked to continue their exercise levels as usual. The period of this phase will last for 14 days.

V. Potential Benefits to You

There are no direct benefits to you associated with your participation in this study. This research study may help to identify possible reactions to the cessation of exercise.

VI. Potential Risks to You

We do not expect the questionnaires and mental tasks to cause you any risk. The blood draws may cause some discomfort, bruising and/or pain at the site of needle insertion. In addition, there is a slight risk of fainting or infection. The tape used for the impedance electrocardiogram may cause some discomfort

as a result of movement restriction during the study tasks. The cold-immersion tasks may cause transient discomfort or pain, but this will disappear as soon as you remove your hand from the cold. If you are not used to biking, your legs may feel tired after the low-level exercise test. There is a potential for a decrease in mood to be associated with the lack of exercise. We ask you to contact the research team if you feel that the research poses too much physical or emotional burden on you.

VII. Right to Withdraw

You may decide to stop taking part in the study at any time. Your relations with the faculty, staff, and administration at USUHS will not be changed in any way if you decide to end your participation in the study. You should let the research team know if you decide to stop taking part in the study. We also reserve the right to remove you from the study at any time at our discretion if circumstances or failure to follow instructions require such actions. If you develop changes in your mood that require professional attention, we will remove you from the study and provide you with a proper referral to a mental health professional.

VIII. Recourse in the Event of Injury

In the event that you suffer physical injury or require hospitalization as a result of participation in this research project, immediate medical treatment will be available at a nearby Department of Defense (military) facility (hospital or clinic). Emergency treatment will be provided even if you are not eligible to receive such care at a military facility. Care will be continued until the medical doctor treating you decides that you are out of immediate danger. If you are not entitled to care in a military facility, you may be transferred to a civilian hospital. The attending doctor or member of the hospital staff will go over the transfer decision with you before it happens. The military will bill your health insurance for health care you receive which is not part of the study. You will not be personally billed and you will not be expected to pay for medical care at our military hospitals.

In case you need additional care following discharge from the military hospital or clinic, a military health care professional will decide whether your need for care is directly related to being in this study. If your need for care is related to the study, the military may offer you limited health care at its medical facilities. If you believe the government or one of the government's employees (such as a military doctor) has injured you, a claim for damages (money) against the federal government (including the military) may be filed under the Federal Tort Claims Act. If you would like to file a claim please contact the University's Office of General Counsel (301-295-3028) and request the filing forms.

If at any time you believe that you have suffered an injury or illness as a result of participating in this research project, you should contact the Office of Research at the Uniformed Services University of the Health Sciences, Bethesda, MD 20814 at (301) 295-3303. This office can review the matter with you, can provide information about your rights as a participant, and may be able to identify resources available to you. Information about judicial avenues of compensation is available from the University's General Counsel at (301) 295-3028.

IX. Privacy and Confidentiality

All information you provide as part of this study will be confidential and will be protected to the fullest extent provided by law. Information that you provide and other records related to this study will be kept private, accessible only to those persons directly involved in conducting this study and members of the Uniformed Services University of the Health Sciences Institutional Review Board (IRB), which provides oversight for protection of human research volunteers. All questionnaires, forms, and audio-tapes will be kept in a restricted access, locked cabinet while not in use. However, please be advised that under Federal Law, a military member's confidentiality cannot be strictly guaranteed. To enhance the privacy of the answers you provide, data from questionnaires will be entered into a database in which individual responses are not identified. After verification of the database information, paper copies of the questionnaires containing identifiers will be shredded. Audiotapes of the interviews will be destroyed at the completion of the study.

You will be paid \$120 for participating in all phases of the study. Payments will be made after completing the study. If you withdraw before the end of the study, you will be paid \$40 for each completed study visit. Active duty military personnel may only be paid for their blood draws. There are three blood draws, so if you complete the study you will be paid \$120. Payments will be made after completing the study. If you withdraw before the end of the study, you will be paid \$40 for each of the blood draws that you have completed.

****IF YOU HAVE ANY QUESTIONS PLEASE FEEL FREE TO ASK THEM****

I have read the explanation of this study in this form. The testing procedures have been reviewed and all my questions have been answered. I understand the nature of the study and I volunteer to participate in it. I attest that I meet the requirements for participation in this study. I understand the study is designed for research purposes and not to be of direct benefit to me.

If you have any additional questions about the study, you should contact:

Dr. Willem Kop at USUHS, Bethesda, Maryland 20814 (301-295-9675) or

Ali Berlin at USUHS, Bethesda, Maryland 20814 (301-295-3522).

They have agreed to discuss the study and the results of your tests with you.

By signing this informed consent, you are agreeing that the study has been explained to you and that you understand the study. You are signing that you agree to take part in this study but you may withdraw your consent to participate at any time without prejudice to future contacts with the Uniformed Services University of the Health Sciences. You will be provided a copy of this consent form.

I AGREE TO PARTICIPATE IN THE FOLLOWING PROCEDURES:

BICYCLE EXERCISE TEST
MEASUREMENT OF HEART RATE
MEASUREMENT OF BLOOD PRESSURE
MEASUREMENT OF LUNG FUNCTION
EXERCISE WITHDRAWAL

BLOOD DRAW
QUESTIONNAIRE
COLD-IMMERSION TASK
COMPUTER TASK
ACTIVITY MONITOR

NAME: _____

SIGNATURE: _____

ADDRESS: _____

WITNESS NAME: _____

SIGNATURE: _____ DATE: _____

I certify that the research study has been explained to the above individual, by my research staff or me, and that the individual understands the nature and purpose, the possible risks and benefits associated with taking part in this research study. Any questions that have been raised have been answered.

PRINCIPAL INVESTIGATOR: _____ **DATE:** _____

Appendix B: Questionnaires and Interview

PANAS

This scale consists of a number of words that describe feelings and emotions. Read each item and then mark the appropriate answer in the space next to the word. Indicate to what extent you have felt this way during the past week. Use the following scale to record your answers.

1	2	3	4	5
very slightly	a little	moderately	quite a bit	extremely
or not at all				

_____ interested	_____ irritable
_____ distressed	_____ alert
_____ excited	_____ ashamed
_____ upset	_____ inspired
_____ strong	_____ nervous
_____ guilty	_____ determined
_____ scared	_____ attentive
_____ hostile	_____ jittery
_____ enthusiastic	_____ active
_____ proud	_____ afraid

POMS

NAME _____ DATE _____ SEX: Male (M) Female (F)		IDENTIFICATION <table border="1" style="margin: auto; border-collapse: collapse;"> <tr><td>1</td><td>2</td><td>3</td><td>4</td><td>5</td><td>6</td><td>7</td><td>8</td><td>9</td><td>0</td></tr> <tr><td>0</td><td>1</td><td>2</td><td>3</td><td>4</td><td>5</td><td>6</td><td>7</td><td>8</td><td>9</td></tr> <tr><td>0</td><td>1</td><td>2</td><td>3</td><td>4</td><td>5</td><td>6</td><td>7</td><td>8</td><td>9</td></tr> <tr><td>0</td><td>1</td><td>2</td><td>3</td><td>4</td><td>5</td><td>6</td><td>7</td><td>8</td><td>9</td></tr> <tr><td>0</td><td>1</td><td>2</td><td>3</td><td>4</td><td>5</td><td>6</td><td>7</td><td>8</td><td>9</td></tr> <tr><td>0</td><td>1</td><td>2</td><td>3</td><td>4</td><td>5</td><td>6</td><td>7</td><td>8</td><td>9</td></tr> <tr><td>0</td><td>1</td><td>2</td><td>3</td><td>4</td><td>5</td><td>6</td><td>7</td><td>8</td><td>9</td></tr> <tr><td>0</td><td>1</td><td>2</td><td>3</td><td>4</td><td>5</td><td>6</td><td>7</td><td>8</td><td>9</td></tr> <tr><td>0</td><td>1</td><td>2</td><td>3</td><td>4</td><td>5</td><td>6</td><td>7</td><td>8</td><td>9</td></tr> <tr><td>0</td><td>1</td><td>2</td><td>3</td><td>4</td><td>5</td><td>6</td><td>7</td><td>8</td><td>9</td></tr> </table>		1	2	3	4	5	6	7	8	9	0	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9
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Below is a list of words that describe feelings people have. Please read each one carefully. Then fill in ONE circle under the answer to the right which best describes HOW YOU HAVE BEEN FEELING DURING THE PAST WEEK INCLUDING TODAY.																																																																																																							
The numbers refer to these phrases. 0 = Not at all 1 = A little 2 = Moderately 3 = Quite a bit 4 = Extremely																																																																																																							
Col (C) O.P. (O)	NOT AT ALL A LITTLE MODERATELY QUITE A BIT EXTREMELY 0 1 2 3 4	NOT AT ALL A LITTLE MODERATELY QUITE A BIT EXTREMELY 0 1 2 3 4	NOT AT ALL A LITTLE MODERATELY QUITE A BIT EXTREMELY 0 1 2 3 4																																																																																																				
	21. Hopeless	0 1 2 3 4	45. Desperate																																																																																																				
	22. Relaxed	0 1 2 3 4	46. Sluggish																																																																																																				
1. Friendly	23. Unworthy	0 1 2 3 4	47. Rebellious																																																																																																				
2. Tense	24. Spiteful	0 1 2 3 4	48. Helpless																																																																																																				
3. Angry	25. Sympathetic	0 1 2 3 4	49. Weary																																																																																																				
4. Worn out	26. Uneasy	0 1 2 3 4	50. Bewildered																																																																																																				
5. Unhappy	27. Restless	0 1 2 3 4	51. Alert																																																																																																				
6. Clear-headed	28. Unable to concentrate	0 1 2 3 4	52. Deceived																																																																																																				
7. Lively	29. Fatigued	0 1 2 3 4	53. Furious																																																																																																				
8. Confused	30. Helpful	0 1 2 3 4	54. Efficient																																																																																																				
9. Sorry for things done	31. Annoyed	0 1 2 3 4	55. Trusting																																																																																																				
10. Shaky	32. Discouraged	0 1 2 3 4	56. Full of pep																																																																																																				
11. Listless	33. Resentful	0 1 2 3 4	57. Bad-tempered																																																																																																				
12. Peeved	34. Nervous	0 1 2 3 4	58. Worthless																																																																																																				
13. Considerate	35. Lonely	0 1 2 3 4	59. Forgetful																																																																																																				
14. Sad	36. Miserable	0 1 2 3 4	60. Carefree																																																																																																				
15. Active	37. Muddled	0 1 2 3 4	61. Terrified																																																																																																				
16. On edge	38. Cheerful	0 1 2 3 4	62. Guilty																																																																																																				
17. Grouchy	39. Bitter	0 1 2 3 4	63. Vigorous																																																																																																				
18. Blue	40. Exhausted	0 1 2 3 4	64. Uncertain about things																																																																																																				
19. Energetic	41. Anxious	0 1 2 3 4	65. Bushed																																																																																																				
20. Panicky	42. Ready to fight	0 1 2 3 4	MAKE SURE YOU HAVE ANSWERED EVERY ITEM. POM 021																																																																																																				
	43. Good natured	0 1 2 3 4																																																																																																					
	44. Gloomy	0 1 2 3 4																																																																																																					

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BDI - II

Date: _____

IU Number: _____

Instructions: This questionnaire consists of 21 groups of statements. Please read each group of statements carefully, and then pick out the one statement in each group that best describes the way you have been feeling during the past week, including today. Circle the number beside the statement you have picked. If several statements in the group seem to apply equally well, circle the highest number for that group. Be sure that you do not choose more than one statement for any group, including Item 16 (Changes in Sleeping Pattern) or Item 18 (Changes in Appetite).

- | | |
|--|---|
| <p>1.
0 I do not feel sad.
1 I feel sad much of the time.
2 I am sad all the time.
3 I am so sad or unhappy that I can't stand it.</p> | <p>6.
0 I don't feel I am being punished.
1 I feel I may be punished.
2 I expect to be punished.
3 I feel I am being punished.</p> |
| <p>2.
0 I am not discouraged about my future.
1 I feel more discouraged about my future than I used to be.
2 I do not expect things to work out for me.
3 I feel my future is hopeless and will only get worse.</p> | <p>7.
0 I feel the same about myself as ever.
1 I have lost confidence in myself.
2 I am disappointed in myself.
3 I dislike myself.</p> |
| <p>3.
0 I do not feel like a failure.
1 I have failed more than I should have.
2 As I look back, I see a lot of failures.
3 I feel I am a total failure as a person.</p> | <p>8.
0 I don't criticize or blame myself more than usual.
1 I am more critical of myself than I used to be.
2 I criticize myself for all of my faults.
3 I blame myself for everything bad that happens.</p> |
| <p>4.
0 I get as much pleasure as I ever did from the things I enjoy.
1 I don't enjoy things as much as I used to.
2 I get very little pleasure from the things I used to enjoy.
3 I can't get any pleasure from the things I used to enjoy.</p> | <p>9.
0 I don't have any thoughts of killing myself.
1 I have thoughts of killing myself, but I would not carry them out.
2 I would like to kill myself.
3 I would kill myself if I had the chance.</p> |
| <p>5.
0 I don't feel particularly guilty.
1 I feel guilty over many things I have done or should have done.
2 I feel quite guilty most of the time.
3 I feel guilty all of the time.</p> | <p>10.
0 I don't cry any more than I used to.
1 I cry more than I used to.
2 I cry over every little thing.
3 I feel like crying, but I can't.</p> |

11.
0 I am no more restless or wound up than usual.
1 I feel more restless or wound up than usual.
2 I am so restless or agitated that it's hard to stay still.
3 I am so restless or agitated that I have to keep moving or doing something.
12.
0 I have not lost interest in other people or activities.
1 I am less interested in other people or things than before.
2 I have lost most of my interest in other people or things.
3 It's hard to get interested in anything.
13.
0 I make decisions about as well as ever.
1 I find it more difficult to make decisions than usual.
2 I have much greater difficulty in making decisions than I used to.
3 I have trouble making any decisions.
14.
0 I do not feel I am worthless.
1 I don't consider myself as worthwhile and useful as I used to.
2 I feel more worthless as compared to other people.
3 I feel utterly worthless.
15.
0 I have as much energy as ever.
1 I have less energy than I used to have.
2 I don't have enough energy to do very much.
3 I don't have enough energy to do anything.
16.
0 I have not experienced any change in my sleeping pattern.

1a I sleep somewhat more than usual.
1b I sleep somewhat less than usual.

2a I sleep a lot more than usual.
2b I sleep a lot less than usual.

3a I sleep most of the day.
3b I wake up 1-2 hours early and can't get back to sleep.
17.
0 I am no more irritable than usual.
1 I am more irritable than usual.
2 I am much more irritable than usual.
3 I am irritable all the time.
18.
0 I have not experienced any change in my appetite.

1a My appetite is somewhat less than usual.
1b My appetite is somewhat greater than usual.

2a My appetite is much less than before.
2b My appetite is much greater than usual.

3a I have no appetite at all.
3b I crave food all the time.
19.
0 I can concentrate as well as ever.
1 I can't concentrate as well as usual.
2 It's hard to keep my mind on anything for very long.
3 I find I can't concentrate on anything.
20.
0 I am no more tired or fatigued than usual.
1 I get more tired or fatigued more easily than usual.
2 I am too tired or fatigued to do a lot of the things I used to do.
3 I am too tired or fatigued to do most of the things I used to do.
21.
0 I have not noticed any recent change in my interest in sex.
1 I am less interested in sex than I used to be.
2 I am much less interested in sex now.
3 I have lost interest in sex completely.

Maastricht Interview of Vital Exhaustion

(If a question is responded positively, ALWAYS inquire about onset of symptom, and increase in severity over the past week)

1. Do you often feel tired? Y / N ____mnth ↑ ↓
For how long have your been feeling tired?
Has it increased lately?
2. Have you felt listless, or without energy lately: Y / N ____mnth ↑ ↓
For how long have you been feeling listless?
Has it increased lately?
3. Do you feel weak all over? Y / N ____mnth ↑ ↓
For how long have you been feeling weak?
Has it increased lately?
4. Have you been irritated more easily? Y / N ____mnth ↑ ↓
When did this start?
Has it increased lately?
5. Do you feel dejected (discouraged)? Y / N ____mnth ↑ ↓
What makes you feel that way?
When did it start?
Does it get worse lately?
6. Do you sometimes feel as if your body is like a battery
that is losing its power? Y / N ____mnth ↑ ↓
When did this start?
Does it get worse?
7. Do you have the feeling that you have not been
accomplishing much lately, or that you are less
capable of accomplishing things? Y / N ____mnth ↑ ↓
When did that start?
Has it increased?
8. Do you ever wake up with a feeling of exhaustion
or fatigue? Y / N ____mnth ↑ ↓
When did that start?
Has it increased?

9. Do you wake up repeatedly during the night? Y / N ____mnth ↑ ↓
 If so, do you take this to be a problem?
 When did that start?
 Did it get worse lately?
10. Do you have the feeling that you cannot cope with everyday problems as well as you used to? Y / N ____mnth ↑ ↓
 When did that start?
 Is it getting harder lately?
11. Do you feel you want to give up trying? Y / N ____mnth ↑ ↓
 When did that start?
 Is it getting harder lately?
12. Have little things irritated you more lately than they used to? Y / N ____mnth ↑ ↓
 When did that start?
 Did it get worse lately?
- (If subject does not report positively, inquire about usual style of handling anger or frustration and if he/she experiences changes in this type of behavior.)
13. Do you blow up more easily than before? Y / N ____mnth ↑ ↓
 When did this start?
 Has it increased lately?
14. Do you have the feeling these days that you just don't have what it takes anymore? Y / N ____mnth ↑ ↓
 When did you start noticing this?
 Have you experienced an increase lately?
15. Have you noticed a decrease in your sexual appetite, or a decrease in the desire to make love? Y / N ____mnth ↑ ↓
 When did that start?
 Has it increased?
16. Has it become harder lately to solve a difficult mental task or problem that requires much attention? Y / N ____mnth ↑ ↓
 When did that begin?
 Has it become worse recently?

17. Do you have increasing difficulty in concentrating on a single subject for long? Y / N ____mnth ↑ ↓
When did this start?
Has it gotten worse lately?

18. Do you shrink from your regular work as if it were a mountain to climb? Y / N ____mnth ↑ ↓
For how long have you been feeling this?
Has it increased lately?

19. Do you believe that you have come to a "dead end"? Y / N ____mnth ↑ ↓
For how long have you been feeling this?
Has it increased lately?

20. Do you sometimes cry or feel like crying? Y / N ____mnth ↑ ↓
When did that start to occur?
Has it increased lately?

21. Do you feel defeated or disillusioned? Y / N ____mnth ↑ ↓
When did this start?
Has it gotten worse lately?

22. Have you experienced a feeling of hopelessness recently? Y / N ____mnth ↑ ↓
For how long have you been feeling this?
Has it increased lately?

23. Would you want to be dead at times? Y / N ____mnth ↑ ↓
For how long have you been feeling this?
Has it increased lately?

24. If applicable:
During our conversation you have described yourself as _____. I understand that this state started ____ months ago. Is that correct? Y / N

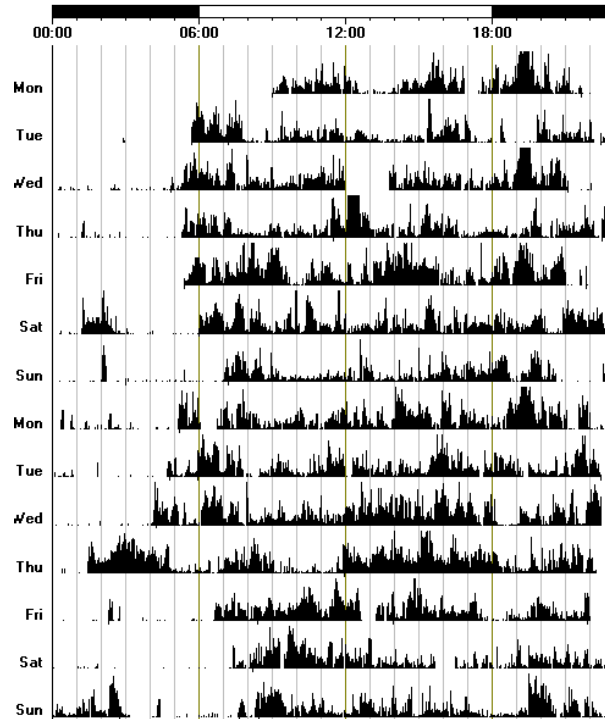
Interviewer impression:

25. Is this state confounded by a medical condition or medication use? Y / N

26. Is there anything else you would like to add about how you have been feeling?

Appendix C – Examples of Actigrams

Control



Exercise-Withdrawn

