THE EFFECTS OF HIGH INTENSITY INTERVAL TRAINING ON SUB-MAXIMAL EXERCISE RESPONSES AND VO_{2max} IN ACTIVE WOMEN TAKING ORAL CONTRACEPTIVES

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THE EFFECTS OF HIGH INTENSITY INTERVAL TRAINING ON SUB-MAXIMAL EXERCISE RESPONSES AND VO$_{2\text{max}}$ IN ACTIVE WOMEN TAKING ORAL CONTRACEPTIVES

A Thesis

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Date

Department of Kinesiology
Abstract

of

THE EFFECTS OF high intensity interval training on sub-maximal exercise responses and VO$_{2\text{max}}$ in active women taking oral contraceptives

by

Jennifer Marie Zierke

Introduction

High intensity interval training (HIIT) leads to improvements in maximal oxygen consumption (VO$_{2\text{max}}$) in 2-weeks (Talanian, 2007). Long term (>4 months) oral contraceptive use (OC) can decrease VO$_{2\text{max}}$ by 11% (Casazza, 2002). It is unknown whether OC can impair exercise training induced adaptations. Therefore, the purpose of this study was to investigate the effects of seven high intensity interval training (HIIT) sessions over 2 weeks on sub-maximal (submax) exercise responses and VO$_{2\text{max}}$ in women taking oral contraceptives.

Methods

Sixteen healthy women of average fitness, VO2max = 40.29 ± 7.51 ml/kg/min, volunteered for this study. The participants were eight women who were taking a monophasic or triphasic OC for > 4 months and eight women who were regularly menstruating and not taking non-oral hormone based contraception were used as the cohort (NOC). Maximal and submax testing at (10% below VT1) were performed on a
cycle ergometer pre and post HIIT. Statistical comparisons were made between OC and NOC to determine the physiological adaptations that occurred with HIIT.

Results

The NOC women had a significant decrease in submax heart rate (HR_{sub}) (148 ± 6.1 vs. 136 ± 4.7 bpm, p=0.02), and an increase in submax oxygen pulse (O_{2pulsesub}) (10.36 ± 0.81 vs. 10.98 ± 0.81 ml/bpm, p=0.02). The OC had a significant increase in submax diastolic blood pressure (dBP_{sub}) (59.7 ± 3.0 vs. 65.2 ± 3.12 mmHg, p<0.01). There were no other significant differences between groups. Post HIIT maximal parameters significantly improved similarly in both groups. Absolute and relative VO_{2max} increased 6.5% (2.6 ± 0.1 vs. 2.8 ± 0.1 L/min, p<0.01) (40.3 ± 1.9 vs. 43.1 ± 1.8 ml/kg/min, p<0.01), peak power increased 6% (226.5 ± 10.37 vs. 241.5 ± 9.2 W p<0.01), and maximal oxygen pulse increased 9.3% (14.14 ± 0.67 vs. 15.26 ± 0.61 ml/beat).

Conclusion

Oral Contraceptive use alters sub-maximal cardiovascular training responses by blunting HR_{sub}, dBP_{sub}, and O_{2pulsesub} adaptations to HIIT, without affecting submax, substrates utilized, or VO_{2max}. The exogenous OC appear to alter sub-maximal cardiovascular function and hemodynamic HIIT training adaptations.

_______________________, Committee Chair
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_______________________
Date

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Chapter 1
INTRODUCTION

The incidence of amenorrhea and oligomenorrhea are higher in female athletes as opposed to their counterparts as a result of high volume exercise training (Yeager, Agostini, Nattiv, & Drinkwater, 1993). This consequently increases their risk of musculoskeletal injury (Drinkwater, Nilsson, Chesnut, Bremner, Shainholts, & Southworth, 1984; Nattiv, 2000). Oral contraceptive pills (OC) are commonly prescribed to athletes to regulate their menstrual cycle to decrease this risk. Although the OC provides several beneficial attributes to all women (cycle regulation, contraception, maintenance of bone density, control of dysmenorrhea, and treatment of oligomenorrhea and amenorrhea) it is of particular interest whether or not the exogenous hormones in the OC affects athletic performance by blunting physiological adaptations to training. The amount of exogenous hormones in OC varies widely and therefore one may have a larger impact on performance than another.

The maximal ability to consume oxygen (VO$_{2\text{max}}$) is dependent on the entire oxygen delivery system, both central and peripheral factors. Maximal oxygen consumption (VO$_{2\text{max}}$) improves with endurance training and is an important indicator of cardiorespiratory fitness (Bassett & Howley, 2000). Decreases in VO$_{2\text{max}}$ from 8% to 11% were reported after 2 to 6 months of monophasic OC use. These decrements were reversed 4 to 6 weeks after subjects discontinued OC (Daggett, Davies, & Boobis, 1983; Notlovitz, Zauner, McKenzie, Suggs, Fields, & Kitchens, 1987). Low dose triphasic OC
decreased VO₂max 4.7% and 13% after two and four months respectively, with no significant changes in maximal ventilation (VE_{max}), maximal heart rate (HR_{max}), or respiratory exchange ratio (RER_{max}) (Casazza, Suh, Miller, Navazio, & Brooks, 2002; Lebrun, Petit, Taunton, & Prior, 2003).

Exogenous oral contraceptives can alter the cardiovascular system and the transport of oxygen and VO₂max. Chronic endurance training increases the body’s oxygen carrying capacity (Red Blood Cell Mass) and decreases blood viscosity (increased plasma) resulting in an increased cardiac output (Q) and blood volume. Thus, blood flow and oxygen to the active muscles are increased during exercise. It has been suggested that high dosed estrogen OC, typically not used today, can increase exercise performance due to reported increases in plasma volume, preload and cardiac output (Lehtovirta, Kuikka, & Pyorala, 1977; Walters & Lim, 1969). In contrast, the newer forms of OC do not support these findings, as the exogenous estrogen dose is much lower. Oxygen pulse (O₂ pulse the amount of oxygen consumed per heart beat) has been reported to decrease with low dose OC (Notelovitz et al., 1987). The reduction in O₂pulse could lead to decrements in VO₂max. In addition OC can alter hemodynamics by increasing resting blood pressure and possibly increasing afterload. (Coney, Washenik, Langley, DiGiovanna, & Harrison, 2001). However, a number of studies have reported no changes in hemodynamics with OC use. (Casazza et al., 2002; Notelovitz et al., 1987; Suh, Casazza, Hornig, Miller, Brooks, 2003; Tantbirojn & Taneepanichskul, 2002).

Recently research has demonstrated that high intensity interval training (HIIT) is a time-efficient way to induce performance adaptations typically seen with regular
endurance training (Gibala, Little, Essen, Wilkin, Burgomaster, Safdar, Raha, & Tarnopolsky, 2006). High intensity interval training at 85-95% VO$_2$max has shown to increase power, time to fatigue, fat oxidation, muscle buffering, and therefore time trial performance in athletes (Acevedo & Goldfarb, 1989; Edge, Bishop, & Goodman, 2006; Stepto, Hawley, Dennis, & Hopkins, 1999; Talanian, Galloway, Heigenhauser, Bonen, & Spriet, 2006; Westgarth-Taylor, Hawley, & Rickard, 1997). In trained athletes the magnitude of the adaptations appear to be smaller than in the untrained. Nonetheless, the adaptations were significant and have an effect on exercise performance in elite and non-elite athletes.

Body composition is an important component of a cyclist’s physical fitness as an optimal power to weight ratio is indicative of better performance. Physiologically an increased body mass or body fat may have a negative impact on exercise performance if significant decreases in muscle mass or increases in weight occur. Reports have shown no significant differences in body composition between fluctuations of endogenous hormones throughout the menstrual cycle or between the inactive and active phases of the OC cycle (Casazza et al., 2002; Lebrun, et al., 1995). However, significant increases in body mass (1kg to 2.4kg) and percent body fat (1% to 6%) have been reported with short and long term monophasic (Notelovitz et al., 1987; Rickenlund, Carlstrom, Ekblom, Brismar, Schoult's, & Hirschberg, 2004) and triphasic use (Casazza et al., 2002; Jacobs, Casazza, Suh, Horning, & Brooks, 2005; Lebrun et al., 2003; Suh et al., 2002). The largest increases in body fat percentage and body mass were reported in studies of longer durational OC use and in subject pools of athletes.
Carbohydrates (CHO) and fatty acids are the dominant fuels oxidized by the muscle for energy production during exercise. The utilization of lipids and CHO as fuels are largely influenced by diet, muscle glycogen content, exercise intensity, exercise duration and gender (Bergman & Brooks, 1999; Coyle, Jeukendrup, Oseto, Hodgkinson, & Zderic, 2001; Horowitz, Mora-Rodriguez, Byerle, & Coyle, 1997; Romijn et al., 1993; Weltan, Bosch, Dennis, & Noakes, 1998; Venables, Achten, & Jeukendrup, 2003). The large variation in fat oxidation among genders remains largely unexplained, but thought to be related to the hormonal differences between males and females. The amount of estrogen and progestogen in OC’s can alter carbohydrate and lipid metabolism at rest (Hackney, Curley, & Nicklas, 1991). During exercise, glycogen is spared when endogenous estrogens and progestogen levels are elevated during the luteal phase of the menstrual cycle. Thus, with exogenous hormone use the elevated estrogen and progestogens may spare glycogen during exercise. However, the research is equivocal reporting both no change in substrate utilization, as well as major shifts from carbohydrate to lipid metabolism and changes in glucose flux (Bemben, Boileau, Bahr, Nelson, & Misner, 1992; Bonen, Haynes, & Graham, 1991; Gillespy, Notelovitz, Ellington, & Kahn, 1991; Jacobs et al., 2004; Lebrun et al., 2003; McNeil & Mozingo, 1981; Notelovits et al., 1987; Suh et al., 2003).

The influence of exogenous and endogenous hormones on cardiovascular responses, maximal oxygen consumption, body composition, and substrate utilization in untrained individuals are well known. It appears that endogenous hormones have little impact in these variables. However, the negative effects of exogenous female hormones
on VO$_{2\text{max}}$, body composition, O$_{2\text{pulse}}$, and blood pressure can limit training adaptations to aerobic exercise. It is possible that training adaptations may still occur with OC use, counteracting the reported decreases in VO$_{2\text{max}}$ and O$_{2\text{pulse}}$, as well as the increases in resting systolic blood pressure, weight, and body fat. High intensity interval training is a time efficient way to induce physiological changes that occur with endurance training. Research specifically evaluating the effects of oral contraceptive use on HIIT adaptations is unknown and necessary for investigation as the results may clarify the effects of OC use on the physiological adaptations to exercise.

Statement of Purpose

The purpose of this study was to investigate the effects of seven high intensity interval training (HIIT) sessions over 2 weeks on sub maximal fat oxidation rates, body composition, hematocrit and VO$_{2\text{max}}$ in women taking oral contraceptives.

Significance of Thesis

To date, research concerning physiological changes in body composition, VO$_{2\text{max}}$, and substrate utilization due to oral contraceptive use are widely available. However, after a comprehensive review of literature, research specifically evaluating how oral contraceptive use effects HIIT adaptations are unknown. Beneficial adaptations to HIIT may be adversely affected in oral contraceptive users. This investigation is important to the field of exercise physiology, as the results indicate that sub-maximal cardiovascular benefits to HIIT are blunted with oral contraceptive use.
Definition of Terms

Amenorrhea: Amenorrhea refers to the absence of three or more menstrual cycles after menarche (American College of Obstetricians and Gynecologists, 2002).

Body Composition: Body composition refers to the chemical composition of the body, often reported as fat mass and fat free mass (muscle, bone and water) (Heyward, 2006).

Endogenous Hormones: Endogenous hormones refer to naturally occurring hormones in the body.

Eumenorrhea: Eumenorrhea refers to a normal menstruation occurring every 25 to 35 days for at least one year (Bryner, Toffle, Ullrich, & Yeater, 1996).

Exogenous Hormones: Exogenous hormones refer to those derived externally from the body.

Follicular Phase: The follicular phase refers to the first half of the menstrual cycle, lasting from cessation of menstrual flow to the surge of luteinizing and follicle-stimulating hormones at the start of the ovulatory phase.

Frank Starling Law: Frank staling law refers to the volume of blood entering the heart during diastole (end-diastolic volume)(EDV), and volume of blood ejected during systolic contraction (stroke volume)(SV). The greater the EDV the greater the SV.

High Intensity Intermittent Training (HIIT): HIIT refers to interval training between an exercise intensity of 80-95% VO_{2max} (Talanian et al., 2007).
Luteal Phase: The third phase of the menstrual cycle, beginning with ovulation and ending with menses.

Maximal Oxygen Consumption (VO$_{2\text{max}}$): Maximal oxygen consumption refers to the maximal amount of oxygen consumed by the whole body during exercise. VO$_{2\text{max}}$ is best described by the Fick Equation, which states that VO$_2$ is equal to cardiac output (HR x SV) and the differences in oxygen content between the arterial and venous blood (a-vO$_{2\text{diff}}$). VO$_{2\text{max}}$ can be measured in absolute or relative terms. Absolute VO$_{2\text{max}}$ is the total amount of oxygen (measured liters per minute) consumed by a subject during a maximal exercise test regardless of the mass of the subject. Relative VO$_{2\text{max}}$ is the maximal amount of oxygen consumed by a subject per kilogram of body weight per minute during exercise (Brooks, Fahey, White, & Baldwin, 2000).

Menstrual Phase: The menstrual phase refers to the phase of the menstrual cycle lasting from the onset of menses to the cession of menstrual flow.

Monophasic Oral Contraceptive: Refers to a pill of a fixed estrogen and progestogen dosage over a 21 day cycle and 7 days of a placebo (Bennell, White, & Crossley, 1999).

Oral Contraceptive: The oral contraceptive pill refers to a pill of exogenous estrogen and progestogen that reduces cycle length variability and provides a 28 day cycle by suppressing the natural production of these hormones through inhibition of pituitary secretion of gonadotropins, thus inhibiting ovulation and preventing pregnancy (Bennell et al., 1999).
Oxygen Pulse (O2 Pulse): The amount of oxygen consumed per heart beat, an indirect measure of stroke volume (VO₂ ml/min ÷ HR)

Rating of Perceived Exertion (RPE): The RPE refers to a rating scale that allows the subject of an exercise test to report the effort needed to perform an exercise task (Borg, 1982).

Sub-maximal exercise: Sub-maximal exercise refers to any exercise intensity that is less than VO₂max (Wilmore, Costill, & Kenny, 2008).

Triphasic Oral Contraceptive: Triphasic oral contraceptives refer to a pill of three different estrogen and progestogen dosages that increases throughout a 28 day cycle (Redman & Weatherby, 2004).

Ventilation Threshold (VT₁): The ventilation threshold refers to the point at which the ventilatory equivalent for oxygen (VE/VO₂) increases with no change in the ventilatory equivalent for CO₂ (VE/VCO₂) (Lucia, Hoyos, Perez, & Chicharro, 2000)

Delimitations

1. The sample was limited to healthy women.
2. The training adaptations were only specific to 2 weeks of HIIT on a cycle ergometer.
3. The types of oral contraceptives utilized were limited to monophasic and triphasic brands.
Limitations

1. The subject and the research assistant were aware of the oral contraceptive being taken.
2. All subjects in the experimental group were taking an oral contraceptive previously prescribed by a physician prior to participating in the study for at least 4 months. The subjects in the control group were not taking an oral contraceptive for at least 4 months prior to participating in the study.
3. The results of the present investigation were limited to healthy women taking monophasic and triphasic oral contraceptives for a minimum of 4 months.

Assumptions

1. All subjects followed pre test protocol for each test administered.
2. All subjects accurately reported dietary intake and physical activity.
3. All subjects maintained habitual physical activity and dietary regimen throughout the course of the study.
4. All OC subjects adhered to prescribed daily OC dosage.
5. The non OC subjects all maintained normal eumenorhemic status.

Hypotheses

1. There was no significant change in fat oxidation rates pre and post HIIT between the NOC and OC subjects.
2. There was no significant change in absolute and relative VO$_{2\text{max}}$ pre and post HIIT between NOC and OC subjects.
3. There was no significant change in hematocrit pre and post HIIT between NOC
4. There was no significant change in body mass pre and post HIIT between NOC and OC subjects.

5. There was no significant change in fat free mass pre and post HIIT between NOC and OC subjects.

6. There was no significant change in fat mass pre and post HIIT between OC and NOC subjects

7. There was no significant change in percent body fat pre and post HIIT between NOC and OC subjects.
Insufficient dietary intake and high intensity exercise training increases a women’s risk of experiencing an abnormal menstrual cycle (Bullen et al., 1985; Loucks, Verdun, & Heath, 1998). Oral contraceptive (OC) are prescribed to both athletes and non-athletes for cycle regulation, contraception, maintenance of bone density, control of dysmenorrhea, and treatment of oligomenorrhea and amenorrhea. The use of OC by female athletes is approximately 47.5% (Anderson, 2003). Dysmenorrhea (painful menstruation) is often due to heavy blood flow which leads to iron deficiency and anemia, which is common in women due to menstrual blood loss (Lebrun et al., 2003; Suedekum & Dimeff, 2005). The prevalence of amenorrhea, due to insufficient secretion of gonadotropin-releasing hormone, is higher in female endurance athletes than non-athletes (Warren & Perlroth, 2001). The resultant decrease in estrogen and progestogen due to amenorrhea can cause an increase in musculoskeletal injuries: bone reabsorption, osteopenia, osteoporosis, and stress fractures (Drinkwater et al., 1984; Nattiv, 2000). The OC maintains the menstrual cycle by maintaining estrogen and progestogen levels, which decreases the risk of anemia and prevents accelerated bone loss (Hergenroeder et al., 1997; Miller & Klibanski, 1999). Although the OC provides several beneficial attributes to women, it is of particular interest whether or not the exogenous hormones in the OC’s affect physiological adaptations to HIIT. The exogenous hormones available in OC vary
widely in dosage and therefore one type of OC may have a larger impact on performance than another.

Types of Exogenous Hormones and Oral Contraceptives

The oral OC is available in many different formulations of exogenous estrogen and progestogen. There is one type of exogenous estrogen (ethinylestradiol) (EE) and 6 types of exogenous progestogens (levonorgestrel, norethindrone acetate, desogestrel, norgestimate, norgestrel, and etynodiol). The dose of exogenous hormones differs between OC brands, and each exogenous progestogen differs in potency. The two types of OC are the combined pill and the mini pill. The combined pill is the most commonly prescribed OC which contains exogenous estrogen, and one of the 6 forms of exogenous progestogen. The mini pill is a progestogen only pill prescribed to women who are breastfeeding or unable to take estrogen due to an elevated risk of heart disease, stroke, and blood clots (Shapiro, 2008). The combined pill is available in three forms: monophasic, biphasic, and triphasic. The monophasic OC is a fixed dosage of exogenous hormones over a 21 day period, followed by 7 days of a placebo. The biphasic OC has a fixed amount of estrogen, but varies in the amount of progestogen twice during a 21 day period, followed by 7 days of a placebo. The triphasic OC most closely resembles the normal menstrual cycle as it contains three separate dosages of exogenous hormones, increasing throughout the 28 day period. These exogenous hormones are believed to cause decreases in VO2max, but it is unclear if adaptations to HIIT are hindered with OC use (Casazza et al., 2002; Lebrun et al., 2003).
Physiological Adaptations to Exercise Training

In previously untrained individuals VO2max increases due to beneficial changes in central and peripheral factors associated with endurance training. The central component of the oxygen delivery system depends upon the maximal cardiac output (Q) and maximal arterial oxygen content. With training blood volume increases and heart rate decreases during exercise at the same absolute intensity. Peripheral factors are related to the extraction of oxygen from the blood (a-v O₂ diff). Skeletal muscle mitochondrial and capillary density increases with training, therefore increasing blood flow, oxygen diffusion and oxygen extraction. Both central and peripheral factors increase the body’s ability to transport oxygen and is expressed as the Fick equation: VO₂max = Qmax x a-v O₂max diff. These variables have been identified in the research to positively affect exercise performance in endurance athletes.

Exercise performance is dependent on many factors, one of which is training. Training induced adaptations have been reported extensively in the literature and are determined by numerous physiological attributes. One of the most prominent adaptations to training is a change in skeletal muscle substrate metabolism (Holloszy & Coyle, 1984). Recently research has demonstrated that sprint interval training is a time-efficient way to induce muscle and performance adaptations similar to endurance training (Gibala et al., 2006). Gibala et al. (2006) compared changes in muscle oxidative capacity, muscle buffering capacity and exercise performance after low-volume sprint interval training (SIT) and high-volume endurance training (ET) in 16 physically active men. The SIT and ET were both conducted over a 2 week period consisting of 6 sessions. The SIT
sessions totaled 2-3 minutes of multiple 30 second Wingate bouts and the ET 90-120 min with 1-2 days recovery between sessions for each group. Six sessions of SIT and ET induced similar improvements in muscle oxidative capacity, muscle buffering capacity (7.6% in SIT and 4.2% in ET) and time trial performance (10.1% in SIT and 7.5% in ET). The current research suggests that both interval and endurance training induce similar changes in exercise capacity and selected muscle adaptations that are related to exercise performance.

High Intensity Interval Training

While athletes employ a variety of training strategies to increase VO2max, recent research suggests that a form of interval training known as HIIT leads to rapid improvements in VO2max and endurance performance in as little as 2-weeks. Such adaptations are typically associated with traditional endurance training. Recently in a study of 8 moderately trained women, VO2max was increased 13% and fat oxidation 36% following 7 sessions of HIIT over a 2 week period at 90% VO2max. Each session consisted of 10 exercise bouts each 4 minutes in duration with a 2 min rest between (Talanian et al., 2006). Edge et al. (2006) reported a 25% increase in muscle buffering capacity after 5 weeks of 4 to 10 bouts for 2 min at 90-100% VO2max in recreationally active women. Acevedo and Goldfarb (1989) showed that increasing training intensity to 90-95% maximal heart rate (MHR) on 3 days out of 6 training days a week for 8 weeks significantly improved time to fatigue and 10-km performance time by about 3 percent and running endurance by 20%, but not VO2max in trained male runners. Stepto et al. (1999) evaluated the effects of different interval training programs on endurance trained
cyclists completing a 40km time-trial, and found that after 6 sessions of eight 4 minute intervals at 85%VO2max with 1.5min rest in 3 weeks showed the greatest increased time trial performance of 2.8%. Similarly Westgarth et al. (1997) examined the effects of sustained HIIT on the athletic performances and fuel utilization in eight male endurance-trained cyclists. Cyclists replaced 15 of their 300 km weeks with 1-2 sessions of HIIT over a six week period. They completed six to nine 5-minute bouts at about 86%VO2max separated by a minute of rest. Maximal power increased 20W and improved 40km time trial speeds by 1.0 km/hr. It appears that in trained male athletes VO2max may not be significantly affected with HIIT as it is with non-trained, but increased fat oxidation and power outputs were exhibited by trained and untrained subjects. The effects of HIIT on female athletes are unknown.

Oral Contraceptives and Physiological Adaptations to Exercise

It is of great concern that the OC might impair exercise induced adaptations in women, and because the monophasic and triphasic OC are most commonly prescribed today their effects on cardiovascular responses, maximal oxygen consumption (VO2max), body composition, and substrate utilization were addressed in this section of the literature review (Anderson, 2003).

Cardiovascular Responses

The cardiovascular system is responsible for the transport of oxygen, delivery of nutrients and removal of waste. During exercise the demand for oxygen to the muscles increases and greater demands are placed on the heart to facilitate oxygen delivery. Cardiac Output (HR x SV), the resistance to blood flow (TPR), blood pressure (sBP,
dBP) and the volume of blood (plasma volume, red blood cell mass) all work synergistically to meet the increased demand for oxygen during exercise. Chronic endurance training improves the efficiency of these mechanisms. Cardiac output (Q) improves with stronger contractions for a given increase in end diastolic volume (Frank Starling law), and increased heart contractility. Increases in blood volume are attributable to both increases in plasma and red blood cells, but because the increased in blood plasma is larger, blood viscosity decreases contributing to increases in blood flow and lower hematocrit values. Blood flow also increases due to decreases in total peripheral resistance (TPR), resulting in a lower blood pressure at a given sub-maximal work rate and a reduced afterload. The combination of these mechanisms facilitates oxygen delivery to the active muscles.

The current research indicates that there is no effect on cardiovascular responses to exercise between phases of the menstrual cycle or the OC cycle. In a comparison study of 16 NOC users, 12 monophasic OC users, and 8 mini pill users, there were no significant differences in heart rate, blood pressure, or cardiac output between the luteal follicular phases of the menstrual cycle or between the inactive and active phases of the OC cycle (Littler, Bojores-Bueno, & Banks 1974). Casazza et al. (2002) and Suh et al. (2003) also reported no significant differences in heart rate or blood pressure during a maximal graded exercise test to exhaustion, in 8 active women between the phases of the menstrual cycle and OC cycle.

Estrogen-induced increases in plasma volume with monophasic OC use could have a beneficial effect during exercise by increasing preload and cardiac output
In fourteen young, healthy women taking a monophasic OC (EE 2.5 mg & Mestranol 0.075 mg) for 2 months, significant increases in blood volume at rest and during exercise were reported as well as increases in plasma volume, stroke volume, and cardiac output, after a 5 minute ride at 80W on a cycle ergometer (Lehtovirta et al., 1977). In a comparison study of 16 NOC users and 12 monophasic OC users, cardiac output was significantly higher in monophasic subjects in comparison to NOC controls (Littler et al., 1974). Walters and Lim (1969) also reported increases in cardiac output after 3 months of OC use in young women taking a monophasic OC as well as significant increases in systolic blood pressure at rest. However, these studies were conducted prior to 1980 when estrogen levels in OC were much higher than the low dose estrogen based OC currently prescribed.

In a more recent investigation using a new low dose monophasic oral contraceptive (EE 0.020 mg, levonorgestrel 0.100 mg) in 349 untrained women reported small but significant increases in resting systolic blood pressure (1.05 mmHg) after 6 months use (Coney et al., 2001). Contrary to this in a comparative study conducted by Tantbirojn and Taneepanichskul (2002) in 140 healthy women, reported no significant differences in resting blood pressure between inactive controls and monophasic (EE 0.03 mg, 0.15 mg levonorgestrel)(EE 0.035mg, 0.25mg levonorgestrel) OC users. In a randomized trial with 12 regularly exercising women (mean VO_{2max} = 42ml/kg/min) using a low dose monophasic OC (EE .035mg, norethindrone 0.4mg) for 6 months reported an 8% decrease in O_{2}pulse, but no significant changes in blood pressure (Notelovitz et al., 1987). The new brands of low dose monophasic OC appear to have
little impact on blood pressure, heart rate and cardiac output during exercise in inactive and active women, but significant decrements in $O_{2}\text{pulse}$. 

Minimal research has been done on cardiovascular responses to triphasic OC use. In 2 studies using eight active women taking a triphasic oral contraceptives for 4 months (EE 0.035mg, norgestimate 0.18/0.215/0.250 mg) there were no significant effects on maximal heart rate or blood pressure reported (Casazza et al., 2002; Suh et al., 2003). In another study using trained women on a triphasic OC (EE 0.035mg, and nortinedrone 0.5mg/1.0mg/0.5 mg) for 2 months also reported no significant differences in maximal blood pressure or heart rate (Lebrun et al., 2003). Based on the minimal amount of cardiovascular research with triphasic OC use, blood pressure and heart rate do not appear to be affected at rest or during maximal exercise, but the effects on sub-maximal exercise and additional cardiovascular responses remain unknown.

Maximal Oxygen Consumption

The maximal ability to consume oxygen is dependent on cardiorespiratory function and the capacity of skeletal muscle mitochondria to consume oxygen. Although $VO_{2}\text{max}$ is not the sole determinant of exercise performance, it is one important predictor of cardiorespiratory fitness, and is the standard for assessing aerobic capacity (Bassett & Howley, 2000; Taylor, Buskirk, & Henschel, 1955). Endurance training increases absolute and relative $VO_{2}\text{max}$ with beneficial changes in cardiovascular responses, fat and carbohydrate oxidation, and body composition. Research has demonstrated that cardiovascular responses, substrate use, and body composition can be influenced by endogenous and exogenous hormones, thereby affecting $VO_{2}\text{max}$.
In a recent study of eight recreationally active women, no significant differences were reported in relative (42.3 ± 0.3ml/kg/min to 42.6 ± 0.2ml/kg/min) or absolute (2.55 ± 0.20L/min to 2.55 ± 0.21L/min) VO$_{2\text{max}}$ between the follicular and luteal phases of the menstrual cycle (Casazza et al., 2002). Further investigations agree with these findings and others have reported a slight, but non-significant decrease (Bemben, Salm, & Salm, 1995; De Souza, Maguire, Rubin, & Maresh, 1990; Lebrun et al., 1995). Casazza et al. (2002), reported that there were no differences in power output, time to exhaustion, ventilation or VO$_2$ during sub-maximal or maximal exercise. Bryner et al. (1995), reported no differences in time to fatigue, VO$_2$, or breathing frequency between the phases of the menstrual cycle in 10 women during a VO$_{2\text{max}}$ test and endurance run at 80%HR$_{\text{max}}$. In a more recent investigation eight healthy women completed a VO$_{2\text{max}}$ test during 3 different phases of the menstrual cycle: low estrogen and progesterone, elevated estrogen and low progesterone, and elevated estrogen and progesterone (Dean, Perreault, Mazzeo, & Horton, 2003). There were no reported differences in VO$_{2\text{max}}$ and time to exhaustion across all 3 phases of the menstrual cycle. Results indicate that endogenous hormones do not appear to have an affect VO$_{2\text{max}}$ or related cardiovascular and respiratory variables. There is also evidence that these variables are not affected between the inactive (IP) and active phases (AP) of the OC cycle (Cassaza et al., 2002; Lynch & Nimmo, 1998).

In seven healthy women (VO$_2 = 35.3$ ml/kg/min) taking a low dose monophasic (EE 0.035mg, 1mg norethindrone) OC for one month, had no affect on VO$_{2\text{max}}$ (Bryner et al., 1996). Daggett et al., (1983) reported an 11% decrease in VO2 max from 44.6 to 39.8
ml/kg/min with 2 months of monophasic OC use which was reversed 6 weeks after subjects discontinued OC use. Six months of monophasic (EE 0.035 mg, 0.4 mg norethindrone) OC use in regularly exercising women decreased absolute VO2max by 8% (2.34 to 2.17 L/min) following 6 months use, and returned to normal after 1 month of OC cessation (Notlovitz et al., 1987).

There have been reported changes in maximal oxygen consumption with both short term and long term triphasic OC use. During two consecutive months of taking low dose triphasic OC in 7 athletic women (50 ml/kg/min), absolute and relative VO2max decreased 4.7% with no significant changes in maximal ventilation (VE\textsubscript{max}), maximal heart rate (HR\textsubscript{max}), or respiratory exchange ratio (RER\textsubscript{max}) (Lebrun et al., 2003). Following 4 months of triphasic OC use in recreationally active women (42.3 ml/kg/min), VO2max decreased 11% (absolute) and 13% (relative) (Casazza et al., 2002). The same study reported a 14% decrease in time to fatigue and an 8% decrease in maximal power output (W\textsubscript{max}), with no significant changes in HR\textsubscript{max}, VE\textsubscript{max}, and RER\textsubscript{max}.

**Body Composition**

Body composition is an important component of physical fitness. It is unclear if reported body mass fluctuations with OC use are due to changes in fat mass or fat free mass. The variability in body composition results were most likely due to premenstrual water retention, training status of subjects, and differences in exogenous hormones prescribed.

During the luteal phase of the menstrual cycle, high concentrations of progestogen result in water and electrolyte loss that stimulates a concurrent increase in aldosterone
concentration. Thus, the rapid decline of circulating progestogen on transition from the luteal to the follicular phase results in excess aldosterone concentrations leading to reported premenstrual water and electrolyte retention. (Gaebelein & Senay, 1982). Therefore, body mass may be elevated due to water retention when both endogenous and exogenous progestogen levels are elevated. This would result in an underestimation of body fat percentage during a hydrostatic weighing as water is considered fat free mass. However, reports have shown no significant differences in body composition between fluctuations of endogenous hormones throughout the normal phases of the menstrual cycle, or between the inactive and active phases of the OC cycle (Casazza et al., 2002; Lebrun, et al., 1995).

The effects of monophasic OC use on body mass and body composition appear to be primarily influenced by the training status of subjects with athletes gaining body mass and sedentary subjects sometimes losing body mass. After 6 months of a monophasic (EE 0.035 mg, nortinedrone 0.4 mg) OC use in active women, increases in body mass of 2 kg were reported while inactive women experienced a 1.5 kg weight loss. Weight returned to baseline after only one month of cessation in the active women (Notelovitz et al., 1987). Similar reports in 140 inactive women taking a monophasic OCs (EE 0.035 mg, norgestimate 0.250 mg, or EE 0.030mg, levonorgestrel 0.150 mg), reported no significant difference in body mass over six months (Tantbirojn & Taneepanichskul, 2002). Following 10 months of low dose monophasic OC use (EE 0.03 mg, .015 mg levonorgestrel) in athletes with amenorrhea and oligomenorrhea (VO2max = 56.7 ml/kg/min), athletes regularly menstruating (VO2max = 55.3 ml/kg/min), and sedentary
controls displayed significant increases in weight of 2.4 kg with no change in lean fat mass in amenorrheic and oligomenorrheic athletes. There were no significant changes reported in regularly menstruating athletes or sedentary controls (Rickenlund et al., 2004).

Lebrun et al. (2003) and Casazza et al. (2002) reported contradicting results when comparing the effects of triphasic OC use on body composition in active women. Lebrun et al. (2003) reported weight gain of 1kg and increases in fat mass by 1% at two months and Casazza et al. (2002) reported no significant changes in body composition after 2 months of OC use, but after 4 months reported a significant increase in body weight of 3% and fat mass of 9%. In two other studies conducted in the same laboratory, using the same oral contraceptive as Casazza et al. 2002, reported an increase in body mass of 1.7% and body fat of 5.6% after 4 months (Suh et al., 2002), and even greater increases were reported after 6 months with significant increases in body mass of 2.5% and body fat of 6% (Jacobs et al., 2005). Though contradicting, it appears that the increases in body mass and body fat percentage occur within the first few months of OC use, without significant fluctuations within the menstrual cycle or OC cycle.

Substrate Utilization

It is well documented that carbohydrates (CHO) and fatty acids are the dominant fuels oxidized by the muscle for energy production during exercise. During low-intensity exercise, lipids provide a greater contribution of energy than that of CHO. As exercise intensity increases the energy contribution from lipids decreases and that from CHO increases (Brooks & Mercier, 1994). The utilization of lipids and CHO as fuels is largely
influenced by diet, muscle glycogen content, exercise intensity, and exercise duration (Bergman & Brooks, 1999; Coyle et al., 2001; Horowitz et al., 1997; Romijn et al., 1993; Weltan et al., 1998). Gender has been reported to influence oxidative metabolism, with women exhibiting higher maximal fat oxidation rates than men (Venables et al., 2003). In a subject pool of 300 trained and untrained men and women, the average exercise intensity for maximal fat oxidation was reportedly higher in women, 52 ± 1 %VO₂max, than in the men, 45 ± 1 %VO₂max. Physical activity, VO₂max, and gender accounted for only 12% of the variation between genders, as percent body fat was not a significant predictor (Venables et al., 2003). Venables et al. (2003) concluded that the variability in substrate utilization could be attributed to training volume, dietary fat intake, muscle glycogen content, and circulating substrates. The failure to control for oral contraceptives in this study could have potentially influenced the female fat oxidation rates due to the high doses of exogenous hormones.

During rest and exercise, research has demonstrated that glycogen is spared when endogenous estrogens and progestogen levels are elevated during the luteal phase of the menstrual cycle because lipid metabolism is favored (Campbell, Angus, Febbraio, 2001; D’Eon et al., 2002; Hackney et al., 1991; Hackney, McCracken-Compton, & Ainsworth, 1994). The amount of estrogen and progestogen in OC’s can has been shown to alter carbohydrate metabolism at rest (Hackney et al., 1991). The current research on OC use during exercise is inconsistent, demonstrating no changes in substrate utilization as well as major shifts from carbohydrate to lipid metabolism.
In seven inactive women taking a low dose monophasic OC, free fatty acid concentrations were consistently higher during mild exercise and the glucose concentrations were lower at rest and during exercise than in the control group (n=8) (Bonen et al., 1991). Similarly in a study of 11 non athletes taking a monophasic OC (Norlestrin 21 (EE 1mg)) reported a shift in substrates utilized during sub-maximal work with an increased reliance on triglycerides and less on glycogen (McNeil & Mozingo, 1981). Eight moderately active women taking a low dose monophasic OC for at least 9 months had lower glucose levels and relied less on carbohydrates during a 90 minute sub-maximal test at 50% VO2max in comparison to 8 NOC users (Bemben et al., 1992).

In a study of 12 regularly exercising young women on a triphasic oral contraceptive (EE 0.035 mg, norethindrone 0.4mg) for 6 months no significant differences were reported in fat metabolism (Notelovits et al., 1987). In a longitudinal study, four months of triphasic OC use in 8 active women did not influence fat oxidation rates at rest or during moderate exercise (Jacobs et al., 2004). Suh et al. (2003) used the same triphasic OC and reported a significant (11%) decrease in glucose appearance and disappearance during moderate intensity exercise. Two months of triphasic OC use (EE 0.030–0.035 mg , nortinedrone 0.5/1.0/0.5 mg) in trained women, had no significant affects on substrate metabolism (Lebrun et al., 2003). In a comparison study of 57 women using two different triphasic OC (levonorgestrel and norethindrone) and 10 controls, reported no significant differences in substrate metabolism (Gillespy et al., 1991).
Summary

It appears that endogenous hormones have little affect on cardiovascular responses, VO$_{2max}$, body composition and substrates utilized during exercise in trained and untrained women. The effects of exogenous hormones on endurance performance in competitive female athletes are less obvious and warrant further investigation. Exogenous hormones in oral contraceptives seem to have an effect on cardiovascular responses at rest and during exercise. Earlier studies have shown that high dose OC use may have adverse affects on the cardiovascular system due to an increased arterial resistance and hypertension, possibly impeding cardiac output. Current low dose brands affect blood pressure to a lesser extent. Endurance training is known to cause a significant decrease in resting blood pressure, which may mask the significant increases reported with OC use (Notelovitz et al., 1987). However, decreases in the amount of oxygen consumed per heart beat (O$_2$ pulse), has been reported with the low dose OC. These increases in blood pressure and decreases in O$_2$ pulse may explain the decreases in maximal oxygen consumption with OC use. Based on the effects of OC use on O$_2$ pulse, VO$_{2max}$, resting BP, and metabolism, a study is warranted to investigate whether these effects will alter the adaptation to HIIT. Increases in body mass and body fat has been attributed to OC use, thus decreasing relative VO$_{2max}$ and power to weight ratio. Exogenous hormones use may have a beneficial effect on substrate metabolism with a greater reliance on fat as a fuel, thus sparing glycogen. These findings provide a basis which to question the value of OC use as a tool to manipulate substrate metabolism for the purpose of athletic competition.
Chapter 3

METHODS

The purpose of this study was to examine the effects of 2 weeks of HIIT on submaximal exercise responses, body composition, hematocrit, and VO₂max in women taking oral contraceptives. A non blinded cross-sectional design was utilized. Physiological variables were collected pre and post HIIT and statistical comparisons were made between OC and NOC users to determine the physiological adaptations that occurred with HIIT.

Subjects

Sixteen physically active women were recruited for this study. The experimental group inclusion criteria required 4 months or greater of monophasic or triphasic OC use. The control group inclusion criteria required females to be eumenorrheic without OC use for 4 months or greater. Each group was composed of 8 women who were equally matched based on relative VO₂max. Each subject completed familiarization trials (hydrostatic weighing and VO₂max), baseline trials (blood work, anthropometric measurements, hydrostatic weighing, VO₂max, and submax), HIIT (7 sessions), and post trials (blood work, anthropometric measurements, hydrostatic weighing, VO₂max, and submax). Subjects were volunteers and classified as low risk according to the American College of Sports Medicine Guidelines (Armstrong et al., 2009). Subjects gave their informed written consent, prior to enrolment in the study (Appendix A). All
experimenatal procedures were explained and questions were answered upon their first visit to the Sac State Human Performance Research Laboratory.

**Procedures**

Subjects reported to the laboratory for testing on twelve separate occasions over a four week period and were instructed to adhere to specific pre-testing procedures. All subjects began testing during the follicular phase defined as 2 to 4 days following the end of menstruation. Subjects were asked to keep a dietary and physical activity log throughout the course of the study to ensure adherence. All variables measured were obtained at the same time of day in a laboratory setting to control for diurnal variation.

Each subject completed a blood profile, anthropometric measurements, hydrostatic weighing with residual volume, sub-maximal endurance trial and a maximal graded exercise test (GXT) pre and post the HIIT. A familiarization VO$_{2\text{max}}$ test and hydrostatic weighing were conducted one week prior to the preliminary testing. A blood draw was used to determine percent hematocrit values. Anthropometric measurements were taken on the leg to measure changes in muscle volume. The hydrostatic weighting with residual volume was used to determine the subjects fat mass (FM) and fat free mass (FFM). The maximal GXT was used to determine maximal values of VO$_2$, ventilation (VE), ventilation threshold (VT), HR, O$_{2\text{pulse}}$, respiratory exchange ratio (RER), and rating of perceived exertion (RPE). The same variables were measured during a 60 minute sub-maximal workload to determine physiological and metabolic responses during steady state exercise. These pre and post maximal and sub-maximal variables were analyzed to measure the physiological and metabolic training adaptations to HIIT.
**Blood Work**

A small (~95 uL) blood sample was collected from a finger stick following a 10 hour fast. The finger stick was performed using a Accu-Check, Safe-T-Pro, sterile, single use lancets (Roche Diagnostics, Indianapolis, Indiana) after sterilizing with single-use alcohol swabs. Blood samples were collected in 90 uL heparinized capillary tubes (Polymer Systems, Indianapolis, Indiana). Blood samples were transferred to the iStat, EC4+ cartridge, which was inserted into the iStat 1, model 300, Portable, Clinical Analyzer (Heska Corporation, Loveland, Colorado) to analyze hematocrit and hemoglobin pre and post HIIT.

**Anthropometric Measurements**

Leg volumes were measured using anthropometrical equations based on skinfold and circumference measurements of the left thigh. (Jones & Pearson, 1969). Skinfold measurements were taken at four locations on the left leg at the anterior thigh in the midline at the 1/3 subishial height level, posterior thigh in the midline at the 1/3 subishial height level, medial calf at the maximal circumference level, and the lateral calf at the maximal circumference level. Circumference measurements were taken at 7 sites on the left leg; gluteal furrow, 1/3 of the subishial height up from the tibial femoral joint space, the minimum circumference above the knee, the maximum circumference around the knee joint space, the minimum circumference below the knee, the maximum calf circumference, and the minimum ankle circumference.
Hydrostatic Weighing with Residual Volume

The residual volume was measured utilizing the nitrogen washout method with the Parvomedics Trueone metabolic measurement system (Sandy, Utah). The gas analyzers were calibrated using a medically certified gas of known concentration (16% O\textsubscript{2}, 4% CO\textsubscript{2}). During the test, subjects re-breathed a 5L bag containing a 100% O\textsubscript{2} mixture using a one way valve inserted into the mouth at the end of SVC maneuver. During the re-breathing procedure O2% and CO2% concentrations were measured using a semipermeable gas sampling line connected to an O\textsubscript{2} and CO\textsubscript{2} analyzer and once equilibrium of gases were obtained the N2 concentrations were recorded and used to calculate RV (Wilmore, Vodak, Parr, Girandola, & Billing, 1980). The direct measurement of residual volume was obtained by averaging three N2 washout trials that were within 5% of each other.

Body composition was measured using the hydrostatic weighing method (Heyward, 2006) with residual volume. Prior to the underwater weighing, residual volume, water temperature, chair tare weight, and subject weight in a swimsuit were obtained. Swimsuits were weighed using a Scout Pro Balance Scale (Ohaus Corporation, Pine Brook, NJ). Subjects entered the hydrostatic weighing tank and sat in a hanging chair. The chair height was adjusted so that water was near neck level. The subjects exhaled air completely while submerging themselves under water. The research assistant then recorded the scale weight to the nearest 0.025 kg and signaled for the subject to return to starting position by shaking the chair. Each subject repeated water submersion at least 3 times or until three weights within 0.1 kg were obtained. The underwater weight
was determined by subtracting the tare weight (chair and swimsuit weight) from the average of the three heaviest recorded weights. The derived body density was used to calculate body fat based on standardized equations for specific populations (Heyward, 2006).

Exercise Tests

Prior to the maximal and sub-maximal exercise tests, the gas analyzers were calibrated using a medically certified gas of known concentration (16% O₂; 4% CO₂). The pneumotach was calibrated across a variety of flow rates (50-80 L/min, 100-200L/min, 200-300L/min, 300-400, >400 L/min) using a calibrated 3L syringe. Inspired and expired O₂ and CO₂ was continuously analyzed by a computerized metabolic cart (ParvoMedics Trueone 2400 metabolic measurement system, Sandy Utah). Exercise tests were all performed on a LODE cycle ergometer (Gronigen, Nederland) and were scheduled at the same time of day. The Lode saddle and handle bar positions were adjusted to replicate the positioning of the subjects own bike. A two way valve (with headgear to hold the mouthpiece) and nose clip was placed on the subject and connected to a pneumotach via a large-bore flexible plastic breathing hose. During the exercise tests, HR was monitored continuously. The rating of perceived exertion (RPE) was obtained using the 6-20 BORG scale (Borg, 1982).

Maximal Graded Exercise Test. The maximal GXT began at 25W or 50W depending on the subjects fitness and increased 25W every minute until volitional fatigue. Subjects rode at their self selected cadence, but the test was terminated if the cadence fell below 60 RPM. The duration of each GXT was between 8-12 minutes to
ensure that proper VO$_{2\text{max}}$ was reached. Respiratory gases were obtained every 30 seconds using the metabolic cart to determine values of VO$_2$, VCO$_2$, ventilation (VE), ventilation threshold ($T_1$), oxygen pulse (O$_2$ pulse), and respiratory exchange ratio (RER). The VO$_2$ max was determined by averaging the last two 30 second values recorded during the GXT. Maximal oxygen consumption was reached if the subject met 2 of the 3 criteria: (1) plateau in VO$_2$ with an increase of $<2\text{ml/kg/min}$, (2) RPE $\geq 17$, and (3) RER $\geq 1.12$. If the subject did not reach two of the three criteria, an additional test was scheduled for another day. Oxygen pulse was calculated based on VO$_2$ and HR at maximal exercise ($\text{VO}_2\text{ml/min/HRbpm}$). Data from the preHIIT GXT trial was used to identify the first ventilation threshold ($T_1$). Threshold one is defined as the point at which the ventilatory equivalent for oxygen (VE/VO2) increases without an increase in the ventilatory equivalent for CO$_2$ (VE/VCO$_2$) (Lucia et al. 2000). The workload corresponding to 10% below $T_1$ workload was the intensity at which the pre and post sub-maximal trials were performed.

*Sub-maximal Exercise Trial.* Based on the analysis of $T_1$, subjects performed a 60 minute Sub-maximal endurance trial pre and post HIIT, at a workload 10% below $T_1$ workload to compare physiological changes related to HIIT. The threshold was determined and agreed upon by two researchers. If an agreement was not reached a third party was asked. Blood pressure was taken and respiratory gases (VO$_2$, VCO$_2$, VE, RER) were collected the last 2 minutes of each 10 minute interval. During this time HR was monitored continuously.
High Intensity Interval Training

Two days following the Sub-maximal trial the subjects began training every other day for 2 weeks, completing 7 HIIT sessions at ~90% \( \text{VO}_{2\text{max}} \) on the Lode cycle ergometer. The appropriate intensity was determined based on the preHIIT maximal GXT. The intensity of HIIT was verified by collecting respiratory gases during sessions 1, 4, and 7. Power output was increased an average of 5W during session 4 to maintain 90% \( \text{VO}_{2\text{max}} \). During session 7, power output was decreased to HIIT1 power to compare HIIT adaptations. Each session consisted of ten 4 min cycling bouts at approximately 90% \( \text{VO}_{2\text{max}} \) with a 2 minute active recovery at 25W between each interval. To characterize the interval sessions, HR, RPE and power measurements were obtained throughout each session.

Statistical Analysis

The experimental data was presented as means and standard deviations. To determine if any significant differences occurred between NOC and OC groups with HIIT pre- and post-test group mean values of \( \text{VO}_{2\text{max}} \), VT, HR, \( \text{O}_2 \) pulse, RER, RPE, body composition, Hct and Hb were analyzed by mixed model repeated measures ANOVA. Sub-maximal values of RER fat oxidation and efficiency (10min values) were analyzed by mixed model repeated measures ANOVA to determine changes with HIIT between OC and NOC groups. The alpha significance level was set at 0.05.
Chapter 4

RESULTS

The current investigation examined the effects oral contraceptive use had on physiological adaptations following 2 weeks of HIIT on hematocrit, body composition, and sub-maximal and maximal exercise parameters. Sixteen (NOC=8, OC=8) healthy females (Age = 26 \pm 3.9 years Ht = 165.59 \pm 4.1 cm Wt = 65.6 \pm 9.5 kg) of average fitness (\(V_{o2max} = 40.2 \pm 7.5 \text{ ml/kg/min}\)) and who regularly exercised 6.2 \pm 3.4 hours per week and 4.53 \pm 1.3 days per week, volunteered as subjects for the study. Seven of the women were taking a monophasic OC (EE 0.03 mg/.035 mg and PG 0.75 mg/1 mg/1.5 mg) and one was taking a triphasic OC (EE 0.03 mg and PG 0.15 mg/1.5 mg/3 mg). All exercise testing was performed in the CSUS Human Performance Research Laboratory.

Table 1: Subject Characteristics

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>26 \pm 3.9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height (cm)</td>
<td>165.59 \pm 4.1</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>65.6 \pm 9.5</td>
</tr>
<tr>
<td>Fat Mass (kg)</td>
<td>15.18 \pm 7.8</td>
</tr>
<tr>
<td>Fat Free Mass (kg)</td>
<td>48.9 \pm 6.1</td>
</tr>
<tr>
<td>Body Fat (%)</td>
<td>22.6 \pm 7.9</td>
</tr>
<tr>
<td>Rest Systolic Blood Pressure (mmHg)</td>
<td>108.8 \pm 6.2</td>
</tr>
<tr>
<td>Rest Diastolic Blood Pressure (mmHg)</td>
<td>65.0 \pm 7.7</td>
</tr>
<tr>
<td>Rest Heart Rate (bpm)</td>
<td>70.6 \pm 13.9</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>39.7 \pm 2.5</td>
</tr>
<tr>
<td>Maximal Oxygen Consumption (ml/kg/min)</td>
<td>40.2 \pm 7.5</td>
</tr>
<tr>
<td>Maximal Power (W)</td>
<td>226 \pm 41.4</td>
</tr>
</tbody>
</table>
Table 2: Description of Female Oral Contraceptive Use

<table>
<thead>
<tr>
<th>Estrogen Dose (mg)</th>
<th>Progesterone Dose (mg)</th>
<th>PG Type</th>
<th>Brand</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.035</td>
<td>1</td>
<td>norethindrone</td>
<td>NECON</td>
</tr>
<tr>
<td>0.03</td>
<td>1.5</td>
<td>norethindrone</td>
<td>Junel</td>
</tr>
<tr>
<td>0.03</td>
<td>3</td>
<td>drospirenone</td>
<td>YAZMINE</td>
</tr>
<tr>
<td>0.035</td>
<td>0.5/0.75/1.0</td>
<td>norethindrone</td>
<td>Ortho Novum 177</td>
</tr>
<tr>
<td>0.03</td>
<td>3</td>
<td>drospirenone</td>
<td>Ocella</td>
</tr>
<tr>
<td>0.03</td>
<td>1.5</td>
<td>norethindrone</td>
<td>Watson</td>
</tr>
<tr>
<td>0.03</td>
<td>3</td>
<td>drospirenone</td>
<td>YAZMINE</td>
</tr>
<tr>
<td>0.03</td>
<td>0.15</td>
<td>levonorgestrel</td>
<td>Levora</td>
</tr>
</tbody>
</table>

Resting Measurements

Baseline and post HIIT resting heart rate (HR), diastolic blood pressure (dBP), and systolic blood pressure (sBP), were not different between trials or groups. Hematocrit concentrations of 40.25% and 39.14% for OC and NOC groups respectively were not significantly different at baseline. Likewise, post hematocrit concentrations of 41.25% and 39.57% in the OC and NOC groups, respectively, were not significantly different from baseline or between groups.
Body Composition

There were no significant differences between body weight (BW), fat free mass (FFM), fat mass (FM), or body fat percentage (BF%) between familiarization and baseline measurements, or between groups throughout all trials. Post high intensity interval training (HIIT) BW, FFM, and calf circumference (CC) were not different from baseline. Repeated measures of ANOVA showed a main interaction between OC and NOC from baseline to post HIIT thigh circumference (figure 4.1). However, the post hoc failed to show significant differences between OC and NOC across the training period. There was a significant decrease in BF% (23.4 ± 2.1% vs. 22.1 ± 2.1% p = .01) (figure 4.2) and FM (15.7 ± 1.9 kg vs. 14.8 ± 1.9 kg p = .02) (figure 4.3) between familiarization and post HIIT trials. There was no difference between baseline and post training. The significance between familiarization and post HIIT BF% and FM, without significance between baseline and post HIIT, could be due to the learning curve associated with the hydrostatic weighing.
Figure 4.1. Average thigh circumference for oral contraceptive (OC) and non oral contraceptive (NOC) groups at baseline and post high intensity interval training (Post HIIT).

* Significant interaction between groups from baseline to post HIIT p<0.05
Figure 4.2. Body fat percentage at familiarization, baseline, and post high intensity interval training (Post HIIT).

* p < 0.05 statistical difference from familiarization
Figure 4.3. Fat mass at familiarization, baseline, and post high intensity interval training (Post HIIT).

* p < 0.05 statistical difference from familiarization
Maximal Exercise

There were significant increases post HIIT training in maximal oxygen consumption (VO₂max L/min and ml/kg/min)(figures 4.6-4.9), peak power (Pₚₐₓ)(figure 4.1), and oxygen pulse (O₂pulseₚₓ)(figure 4.11). There were no significant differences in outcomes between oral contraceptive (OC) and non oral contraceptive (NOC) groups post HIIT. Post HIIT RPEₚₓ, RERₚₓ, and VEVO₂ₚₓ did not change between any of the trials.

Maximal heart rate (HRₚₓ) significantly decreased (figure 4.4) from familiarization to post HIIT (186.7 bpm vs. 183.9 bpm p=0.01), but did not differ from baseline to post HIIT. Maximal ventilation (VEₚₓ) significantly increased (figure 4.5) from familiarization to post HIIT (102.3 L/min vs. 108.4 L/min p=0.04), with no differences between baseline to post HIIT. Post HIIT absolute (figures 4.6-4.7) (2.6 L/min vs. 2.6 L/min vs. 2.8 L/min p<0.01) and relative VO₂ₚₓ increased (figures 4.8-4.9) (39.6 ml/kg/min vs. 40.3 ml/kg/min vs. 43.1 ml/kg/min p<0.01), Pₚₓ (figure 4.10) (223.3 W vs. 226.5 W vs. 241.5 W p<0.01), and O₂pulse (figure 4.11) (13.8 ml/min/beat vs. 14.1 ml/min/beat vs. 15.3 ml/min/beat p<.01) were all significantly higher from familiarization and baseline.
**Maximal Heart Rate**

*Figure 4.4.* Maximal heart rate at familiarization, baseline and post high intensity interval training (HIIT).

* p < 0.05 statistical difference from familiarization
Maximal Ventilation

Figure 4.5. Maximal ventilation (VE) at familiarization, baseline and post high intensity interval training (HIIT).

* p < 0.05 statistical difference from familiarization
Maximal Absolute VO2

Figure 4.6. Maximal absolute oxygen consumption (VO$_{2\text{max}}$ L/min) at familiarization, baseline and post high intensity interval training (HIIT).

* p < 0.05 statistical difference from familiarization

** p < 0.05 statistical difference from baseline
Maximal Absolute VO2 Between Groups

Figure 4.7. Maximal absolute oxygen consumption (VO2max L/min) at familiarization, baseline and post high intensity interval training (HIIT) in oral contraceptive (OC) and non oral contraceptive (NOC) groups. There were no significant interactions between groups (p>0.05).
**Figure 4.8.** Maximal relative oxygen consumption (VO$_{2\text{max}}$ ml/kg/min) at familiarization, baseline and post high intensity interval training (HIIT).

* $p < 0.05$ statistical difference from familiarization

** $p < 0.05$ statistical difference from baseline
Figure 4.9. Maximal relative oxygen consumption (VO₂<sub>max</sub> ml/kg/min) at familiarization, baseline and post high intensity interval training (HIIT) in oral contraceptive (OC) and non oral contraceptive (NOC) groups. There were no significant interactions between groups (p>0.05).
Maximal Power

Figure 4.10. Maximal power (Watts) at familiarization, baseline and post high intensity interval training (HIIT).

* p < 0.05 statistical difference from familiarization

** p < 0.05 statistical difference from baseline
Maximal Oxygen Pulse

Figure 4.11. Maximal oxygen consumed per beat of the heart (O₂pulse ml/min/beat) at familiarity, baseline and post high intensity interval training (HIIT).

* p < 0.05 statistical difference from familiarization

** p < 0.05 statistical difference from baseline
Sub-maximal Exercise

During the sixty minute sub-maximal exercise trial absolute VO$_2$ (figures 4.12), relative VO$_2$ (figure 4.13), VE (figure 4.14), and sBP (figure 4.15) were not different between groups and did not change with training from baseline. However, these variables significantly increased with time among all participants in both trials. There were no differences in VE/VO$_2$ over time, between groups, or from baseline to post HIIT.

There was a training and time interaction on rating of perceived exertion (RPE) (p=.04), which significantly increased over time in both trials and groups and decreased significantly with training (figure 4.16). There was a time interaction for RER (p< 0.01) and rate of CHO use (p<0.01) and FAT use (p<0.01). Respiratory Exchange ratio (RER) and rate of CHO oxidation decreased and FAT oxidation increased significantly with time after 30 min during baseline and post HIIT sub-maximal trails, with no differences between trials or groups (figures 4.17,4.18, 4.19, 4.20).

There was a training and group interaction between sub-maximal O$_2$ pulse and HR. Sub-maximal oxygen pulse was significantly higher post HIIT in the NOC group (p=0.02)(figure 4.21), and was not different in the OC group. The sub-maximal HR significantly decreased (p=0.01)(figure 4.22) in the NOC group with training and did not change in the OC group. There was a time, training and group interaction in sub-maximal dBp. Diastolic blood pressure was significantly higher throughout the 60 minute sub-maximal exercise trial in the OC group post HIIT (p<0.05) (figure 4.23,4.24), with no changes in the NOC group.
Sub-maximal Absolute VO2

* p < 0.05 statistical difference from 10min

** p < 0.05 statistical difference from 20min

Figure 4.12. Absolute VO2 (L/min) over a 60 minute sub-maximal exercise trial.
Sub-maximal Relative VO2

* p < 0.05 statistical difference from 10min

** p < 0.05 statistical difference from 20min

*** p < 0.05 statistical difference from 30min

Figure 4.13. Relative VO₂ (ml/kg/min) over a 60 minute sub-maximal exercise trial.
Figure 4.14. Ventilation (L/min) over a 60 minute sub-maximal exercise trial.

* p < 0.05 statistical difference from 10min
Figure 4.15. Systolic blood pressure (sBP) over a 60 minute sub-maximal exercise trial.

* p < 0.05 statistical difference from 10min
Figure 4.16. Rating of perceived exertion (RPE) over a 60 minute sub-maximal exercise trial at baseline and post high intensity interval training (HIIT).

* p < 0.05 statistical difference from baseline
Figure 4.17. Respiratory exchange ratio (RER) over a 60 minute sub-maximal exercise trial.

* p<0.05 significantly different from 10 min
* p<0.05 significantly different from 20 min
* p<0.05 significantly different from 30 min
Figure 4.18. Respiratory exchange ratio (RER) over a 60 minute sub-maximal exercise trial at baseline and post high intensity interval training (HIIT) in both oral contraceptive (OC) and non oral contraceptive (NOC) groups. There were no significant interactions between groups (p>0.05).
Figure 4.19. Rate of carbohydrate (CHO) oxidation during a 60 minute sub-maximal exercise trial.

* p<0.05 significantly different from 10 min

* p<0.05 significantly different from 20 min
Figure 4.20. Rate of fat oxidation during a 60 minute sub-maximal exercise trial at baseline and post high intensity interval training (HIIT).

* p<0.05 significantly different from 10 min

* p<0.05 significantly different from 20 min

* p<0.05 significantly different from 30 min
Sub-maximal Oxygen Pulse Between Groups

Figure 4.21. Mean sub-maximal oxygen pulse (O₂ pulse) at baseline and post high intensity interval training (HIIT) in oral contraceptive (OC) and non oral contraceptive (NOC) groups.

* p < 0.05 statistical difference from baseline in NOC group
Figure 4.22. Mean sub-maximal heart rate at baseline and post high intensity interval training (HIIT) in oral contraceptive (OC) and non oral contraceptive (NOC) groups.

* p < 0.05 statistical difference from baseline in NOC group
Sub-maximal dBP Between Groups Over Time

*Figure 4.23.* Diastolic blood pressure (dBP) over a 60 minute sub-maximal exercise trial at baseline and post high intensity interval training (HIIT) in both oral contraceptive (OC) and non oral contraceptive (NOC) groups.

* p<0.05 statistical significance from baseline in OC
Figure 4.24. Average 60 minute sub-maximal diastolic blood pressure (dBP) during baseline and post high intensity interval training (HIIT) trials in oral contraceptive (OC) and non oral contraceptive (NOC) groups.

* p<0.05 statistical significance from baseline
High Intensity Exercise

The HIIT metabolic gases were compared and analyzed between sessions 1, 4, and 7. The heart rate (HR) and rating of perceived exertion (RPE) were compared and analyzed between all 7 interval sessions. Power was significantly increased ($p = 0.002$) in the NOC group from $153.1 \pm 12.2\ W$ to $157.6 \pm 11.9\ W$, and did not increase in the OC group (figure 4.25). Absolute and relative VO$_2$ was significantly different between HIIT sessions 4 and 7 ($2.37 \pm 0.1\ L/min$ vs. $2.30 \pm 0.1\ L/min$ $p=0.03$ and $36.4 \pm 1.7$ vs. $35.3 \pm 1.7\ ml/kg/min \ p=0.04$), but not between groups (figure 4.26 and 4.27). There was a significant decrease in ventilation between trials 1 to 7 ($76.0 \pm 2.12\ L/min$ to $66.7 \pm 2.5\ L/min \ p<0.01$), and from 4 to 7 ($75.00 \pm 2.5\ L/min$ vs. $66.7 \pm 2.5\ L/min \ p<0.01$), with no difference between groups (figure 4.28). Ventilation equivalents (VEVO$_2$) significantly decreased from trials 1 to 7 ($32.6 \pm 1.1$ vs. $29.0 \pm 0.7\ p<0.01$) and between trials 4 to 7 ($32.3 \pm 1.0$ vs. $29.0 \pm 0.7\ p=0.01$), with no difference between groups (figure 4.29). There was a significant increase in O$_2$pulse from trials 1 to 4 ($13.4 \pm 0.6\ ml/min/beat$ to $13.9 \pm 0.6\ ml/min/beat\ p=0.02$) and trials 1 to 7 ($13.4 \pm 0.6\ ml/min/beat$ vs. $13.9 \pm 0.6\ ml/min/beat\ p=0.01$), with no differences between groups (figure 4.30). There were no differences in RER between trials or groups. Heart rate was significantly lower in both groups from IIT session 1 to 3 ($175.1 \pm 2.3\ bpm$ vs. $165.9 \pm 2.2\ bpm \ p=0.03$), and 1 to 5 ($175.1 \pm 2.3\ bpm$ vs. $169.8 \pm 2.0\ bpm \ p=0.01$), 1 to 6 ($175.1 \pm 2.3\ bpm$ vs. $167.9 \pm 2.3\ bpm \ p<0.01$), and 1 to 7 ($175.1 \pm 2.3\ bpm$ vs. $165.9 \pm 2.3\ bpm \ p<0.01$). The power was increased during session four which caused an increase in heart rate. Despite this adjustment, HR decreased from baseline to session 6. Heart rate was also significantly
lower from trial 2 to 7 (171.6 ± 2.3 bpm vs. 165.9 ± 2.3 bpm p=0.01) and 4 to 7 (172.1 ± 2.2 bpm vs. 165.9 ± 2.3 bpm p<0.01) (figure 4.32). Rating of perceived exertion (RPE) was significantly lower despite the increase in power from trials 1 to 6 (16.5 ± 0.4 vs. 14.8 ± 0.3 p<0.01), 1 to 7 (16.5 ± 0.4 vs. 14.4 ± 0.3 p<0.01), 4 to 7 (15.8 ± 0.4 vs. 14.4 ± 0.3 p=0.01), and 5 to 7 (15.6 ± 0.4 vs. 14.4 ± 0.3 p=0.04) (figure 4.32).
HIIT Power Between Groups

Figure 4.25. High intensity interval training (HIIT) power (W) during session 1, 4, and 7.

* $p < 0.05$ statistical difference in NOC group from HIIT1

**$p < 0.05$ statistical difference in NOC group from HIIT7
Figure 4.26. High intensity interval training (HIIT) absolute VO\(_2\) (L/min) during session 1, 4, and 7.

* p < 0.05 statistical difference from HIIT 4
HIIT Relative VO2

* p < 0.05 statistical difference from HIIT 4

* Figure 4.27. High intensity interval training (HIIT) relative VO2 (ml/kg/min) during session 1, 4, and 7.
Figure 4.28. High intensity interval training (HIIT) ventilation (VE) (L/min) during session 1, 4, and 7.

* p < 0.05 statistical difference from HIIT1

** p < 0.05 statistical significance from HIIT4
Figure 4.29. High intensity interval training (HIIT) ventilation equivalents (VE/VO$_2$) during session 1, 4, and 7.

* p < 0.05 statistical difference from HIIT1

** p < 0.05 statistical significance from HIIT4
HIIT Oxygen Pulse

Figure 4.30. High intensity interval training (HIIT) oxygen pulse ($O_2$pulse) during session 1, 4, and 7.

* p < 0.05 statistical difference from HIIT1
Figure 4.31. High intensity interval training (HIIT) heart rate (HR) throughout all 7 sessions.

* p < .05 statistical difference from HIIT1

** p < 0.05 statistical significance from HIIT2

*** p < 0.05 statistical significance from HIIT4
Figure 4.32. High intensity interval training (HIIT) rating of perceived exertion (RPE) throughout all 7 sessions.

* p < 0.05 statistical difference from HIIT1

** p < 0.05 statistical significance from HIIT4

*** p < 0.05 statistical significance from HIIT5
The results of the current study indicate that the hypotheses, sub-maximal fat oxidation will be different between groups post HIIT, increases in absolute and relative VO_{2\text{max}} will be different between groups post HIIT, increases in hematocrit will be different between groups post HIIT, body mass changes will be different between groups post HIIT, fat free mass will be different between groups post HIIT, fat mass will be different between groups post HIIT, and body fat percentage will be different between groups post HIIT were not supported.
The current investigation was the first to evaluate the effects of 2 weeks of HIIT on sub-maximal, high intensity, and maximal exercise parameters in women using OC. Seven of the women were taking a monophasic OC (EE 0.03 mg/0.035 mg and PG 0.75 mg/1 mg/1.5 mg) and one was taking a triphasic OC (EE 0.03 and PG 0.15 mg/1.5 mg/3 mg). The OC used in this study are similar to those used in research conducted after 1980 (EE 0.2 mg/0.03 mg/0.35 mg & PG 0.1 mg/0.15 mg/0.18 mg/0.215 mg/0.250 mg/0.4 mg/0.5 mg/1.0 mg) (Casazza et al., 2002; Notelovitz et al., 1987; Lebrun et al., 2003; Suh et al., 2003 Tantbirojn & Taneepanichskul, 2002). Oral contraceptives had much higher dosages of estrogen (2.5 mg/3 mg) prior to the early 1980’s (Lehtovirta et al., 1977; Littler et al., 1974; Walters & Lim, 1969). Sub-maximal cardiovascular responses were improved in NOC women, and blunted in OC women. Sub-maximal $O_2$ pulse was significantly higher and $HR_{sub}$ was significantly lower post HIIT in the NOC group, and $dBP_{sub}$ was significantly higher in the OC group. Sub-maximal oxidation rates of fat and carbohydrates were unaltered with HIIT in both groups. Both groups’ HIIT and maximal responses were similar with increases in $O_2$ pulseHIIT, $VO_2max$, $P_{max}$, and $O_2$ pulse max, and decreases in $HR_{HIIT}$ and RPE HIIT, with the exception of a significant increase in HIIT power in the NOC group. Body composition (FM, FFM, BF%) were unaltered in NOC and OC groups post HIIT, which was agrees with previous research conducted on regularly menstruating women (Rickenlund et al., 2004).
Seven sessions of HIIT were completed over the two weeks and physiological variables from session 1 and 7 were compared. During session 4 HIIT power increased an average of 5W in order to maintain 90% VO2 during the training in the NOC group, with no significant increases in the OC group. This is less then the 19W increase reported from training sessions 1-6 in a similar investigation (Talanian et al., 2007). However, the previous study made adjustments in power throughout all sessions based on HR, whereas the present investigation adjusted power based on relative VO2. Despite this, heart rate decreased to a greater extent (5.3%) in this study compared to Talanian (2.5%) (Talanian et al., 2007). These findings confirm the rapid adaptations in training responses observed with HIIT. It appears that OC do not significantly alter the training adaptations associated with HIIT in comparison to NOC.

High intensity interval training is an established rapid method of improving endurance performance. Increases in stroke volume and decreases in HR at a given workload have been contributed to endurance training. Based on the minimal amount of cardiovascular research with OC use, blood pressure and heart rate do not appear to be affected at rest or during maximal exercise, but the effects on sub-maximal exercise and additional cardiovascular responses remain unclear. In this study expected adaptations to HIIT were observed in the NOC women. Sub-maximal oxygen pulse, which is an indirect measure of stroke volume, increased 5.6% in the NOC group, and was unaltered in the OC group. These findings are contrary to research conducted prior to 1980 in which estrogen-induced increases in plasma volume with OC use was believed to have a beneficial effect during exercise by increasing preload and cardiac output (Lehtovirta et
al., 1977; Littler et al., 1974; Walters & Lim, 1969). However, the doses of estrogen in these studies were much higher (EE 2.5 mg/ EE 3.0 mg) than those currently prescribed and used in this study (EE 0.03 mg /0.035 mg). In a more recent investigation that used similar OC (EE 0.03 mg/ 0.035 mg, PG 0.4 mg) and subjects (VO$_2$max = 42 ml/kg/min) reported an 8% decrease in O$_{2\text{pulsem}ax}$ in OC women (Notelovitz et al., 1987). In the current investigation O$_{2\text{pulsem}ax}$ was not blunted in OC women and increased 8% in both groups post HIIT. The increases in the NOC groups O$_{2\text{puslesub}}$ coincided with an 8% reduction in HR$_{\text{sub}}$. The OC group demonstrated no sub-maximal cardiovascular improvement with HIIT, and had an 11% increase in dBP$_{\text{sub}}$ with no changes in O$_{2\text{pulse}}$. However, maximal cardiovascular responses were similar between groups. The difference in O$_{2\text{pulsesub}},$ HR$_{\text{sub}},$ and dBP$_{\text{sub}}$ between NOC and OC groups, indicate possible alterations in vascular resistance and hemodynamics. These results specifically point to a decreased stroke volume (decrease O$_{2\text{pulse}}$) due to increases in vascular tone (increased dBP) with a compensatory maintenance of HR, despite large increases in cardiovascular capacity (increased VO$_2$max).

The alterations in vascular resistance and hemodynamics are consistent with OC effects on the nitric oxide (NOS) and renin angiotensin (RAS) system. L-arginine infusion has been reported to reduce vascular resistance at a lower dose in NOC (250 mg/kg), than in OC users (500 mg/kg) (Cherney, Scholey, Cattran, Zimpelmann, Kennedy, Lai, Burnes, & Miller, 2007). In OC women, this study reported increased levels of angiotensin II and aldosterone, which are important regulators of the RAS. Activation of RAS would result in an increased vascular resistance and blood pressure
due to increased renin, angiotensin, and aldosterone. In women taking OC, the nitric oxide system (NOS) was up regulated to maintain resting blood pressure and required a much larger dose (200%) of L-arginine to reduce vascular resistance. The effects of OC on cardiovascular resistance would explain the changes during exercise observed in our study. During maximal exercise there is a maximal vasodilation effect, which allows maximal blood flow. This would explain why maximal cardiovascular responses were similar between groups. However, during sub-maximal exercise there is only a moderate vasodilation stimulus to reduce TPR. Because NOS and RAS are already up regulated in OC users at rest, moderate vasodilation during sub-maximal exercise is blunted. This would explain the increases in dBP_{sub} (TPR) without changes HR_{sub} or O_2pulses_{sub}. These findings suggest that the elevated estrogens and progesterone’s in OC reduce the cardiovascular training adaptations normally observed in HR_{sub}, O_2pulses_{sub} and dBP_{sub} during aerobic conditioning in recreationally active women.

Oral contraceptive use does not appear to alter fat or carbohydrate oxidation rates at rest or during exercise (Jacobs et al., 2004; Lebrun et al., 2003; Notelovits et al., 1987). However, we expected an improvement in fat oxidation with HIIT as reported by Talanian (Talanian et al., 2007). It was surprising that there were no improvements in sub-maximal whole body fat oxidation. This indicates that in women of higher fitness (VO2max=40.2±7.5 ml/kg/min) and greater training specificity (6.2 ± 3.4 hours of cycling per week), such as the women in the current investigation, have no improvements in fat oxidation. Our findings suggest that improvements in fat oxidation in women may be dependent on initial cardiovascular fitness and total hours of aerobic activity.
In the present investigation absolute and relative VO$_{2\text{max}}$ increased 6.5%, following 2 weeks of HIIT, with no differences between OC and NOC groups. This is half that of the previously reported 13% increase in VO$_{2\text{max}}$ by Talanian (Talanian et al., 2007). An equivalent increase in VO$_{2\text{max}}$ between groups was not expected since decreases in VO$_{2\text{max}}$ from 8% to 13% were reported after 2 to 6 months of similar OC use (EE .035 mg, PG 0.4mg ) and subjects’ fitness levels (VO$_{2\text{max}}$ 42.3 ml/k/min) (Casazza et al., 2002; Daggett et al., 1983; Notlovitz et al., 1987). However, the authors in the Talanian study did not report whether these women were taking OC. The current investigation was a comparison of training adaptations with NOC verses OC use. The women in this study were on OC or NOC for at least 4 months prior to the study. A limitation of this study was that we could not measure changes in VO$_{2\text{max}}$ with initial OC use. The smaller differences observed in VO$_{2\text{max}}$ could have been attributed to the higher training status and cardiovascular fitness (VO$_{2\text{max}}$ 10% higher) of the subjects in this study. Maximal power increased 15W, which agrees with a 20W increase reported in a similar HIIT protocol (5-minute bouts at about 86%VO$_{2\text{max}}$ separated by a minute of rest) with eight male endurance-trained cyclists (Westgarth et al., 1997). Maximal O$_2$pulse increased 7.3% after HIIT training in both groups. Notelovitz et al. (1987), reported an 8% decrease in O$_2$pulse$_{\text{max}}$ in women taking OC (EE 0.035 mg, norethindrone 0.4mg) with a 9% increase in NOC women of similar fitness (VO$_{2\text{max}}$ 42 ml/kg/min) taking a low dose monophasic OC. The dosage (EE 0.03mg/ .035mg and PG 0.15 mg/0.75 mg/1.0 mg/1.5 mg/ 3.0 mg) and fitness level (VO$_{2\text{max}}$ 40.2±7.5 ml/kg/min) of the subjects in the current investigation were similar to those of Notelovitz et al. (1987). Women taking oral
contraceptives have similar maximal parameters following 2 weeks of HIIT compared to NOC females. Based on these findings it appears the magnitude of adaption in VO2max is similar in women taking OC.

Conclusion

As demonstrated by the NOC group, endurance training is known to cause a significant decrease in resting blood pressure and heart rate. In contrast, the physically active OC subjects in the current investigation did not have significant alterations in hemodynamics at rest. Furthermore, sub-maximal cardiovascular adaptations associated with 2 weeks of HIIT are reduced with OC use in comparison to NOC. The NOC women experienced normal sub-maximal exercise adaptations to training with reductions in HR_{sub} and increases in O_2pulsesub. In comparison the OC women had no changes in HR_{sub} or O_2pulsesub, but had an increase in dBP_{sub}. However, similar increases in maximal exercise capacity and O_2pulsem_{ax} were reported in the current study and by others. Oral contraceptives do not limit maximal physiological adaptations to 2 weeks of HIIT (Notevitz et al., 1987). Although increases in fat oxidation with HIIT were reported in recreationally active women, our results indicate that substrate utilization is unaltered in women of higher fitness with greater training specificity (Talanian et al., 2007). A limitation of this study was that the women were previously taking OC for a minimum of four months. Therefore the exact impact of OC use on pre OC cardiovascular parameters prior to HIIT in our female subjects were unknown. It is apparent that sub-maximal exercise cardiovascular responses are reduced with long term monophasic OC use in premenopausal recreationally active women following 2 weeks of HIIT. Based on the
sub-maximal cardiovascular responses, the elevated estrogens and progesterone’s found in OC may alter long term (>2weeks) sub-maximal exercise responses to training in women.

The effects of OC use on prolonged sub-maximal endurance training (>2 weeks) warrant further investigation. Further research of the sub-maximal cardiovascular responses to HIIT are suggested to determine the underlying reduction in cardiovascular adaptations associated with OC use. Specifically research of the changes in peripheral resistance (NOS & RAS & TPR) and cardiac function (SV) are warranted. The results of this study can only be generalized to moderately physically active premenopausal women of average fitness. The effects of OC use on exercise performance and in postmenopausal women remain to be investigated.
APPENDIX A

Informed Consent
Consent to Participate in the

Adaptive Responses to High Intensity Interval Training in Moderately Trained Women Taking Oral Contraceptives

Professor Roberto Quintana in the Kinesiology Department at Sacramento State, and exercise physiology graduate research assistant Jennifer M. Zierke would like to compare the effects of high intensity interval training on exercise capacity in moderately trained women taking oral contraceptives versus non oral contraceptive users. You are invited to participate in a research study titled, “The Adaptive Response to High Intensity Interval Training in Moderately Trained Women Taking Oral Contraceptives”. You were selected as a possible participant for this study because of your current health status and your interests in participating in this research.

Explanation of the Treatments and Tests to Be Administered

If you decide to participate, Roberto Quintana, Ph.D. will require you to report to the Human Performance Laboratory (HPRL) on 12 occasions to complete several tests. The procedures involved are explained as follows:

A. You will report to HPRL to fill out a medical history questionnaire and have vital signs measured to determine whether you are suitable for enrollment in the study. Also during this time you will be able to become familiar with the procedures of the study and equipment that will be used. This will require a familiarization with body composition testing (underwater weighing) and a maximal aerobic capacity testing.

B. On two separate days you will report to the HPRL to complete additional testing. On the 2nd visit, a small capillary finger stick will be taken to assess hematocrit and hemoglobin values (less than 0.95 uL) followed by a cycling test. The cycling test is an incremental cycle ergometer exercise test until you reach maximal fatigue. The cycling test will last 10-16 minutes. Your HR and oxygen consumption will be measured every stage of the exercise tests. On the 3rd visit, a one hour sub-maximal exercise test at a moderate intensity will be conducted. During this test HR, and expired gas exchange will be measured every 10 minutes.

C. Following the above tests, you will be enrolled in the exercise training portion of the study. The training consists of performing 7 high intensity interval exercise bouts over a 14 day period on a cycle ergometer. The intervals performed will be ten-4 min intervals on a cycle ergometer with 4 minutes of rest in between each bout.

D. After the high intensity interval training is completed, the measurements described in Section B will be repeated to assess changes in exercise capacity and metabolism resulting from the training.

E. The total time commitment for the study will be approximately 24 hours over five weeks.

Risks: Drawing capillary blood with a finger stick is associated with risks of infection, pain and bruising. You might get light headed or develop a bruise at the sampling site (10%). Risk of infection will be minimized by using sterile technique and by following aseptic procedures. A total of ~0.6 mL will be drawn over the entire course of study. If
any adverse reactions occur due to the blood draw, you will be referred to your personal physician or the CSUS Student Health Center if you are a CSUS student.

Exercise tests to the point of fatigue are associated with a risk of death (<0.01%) and complications with the heart (<0.1%) (i.e. irregular heart rhythm, inadequate blood to the heart, and heart attack). The risk of incidents occurring is much less for individuals who are young, exercise regularly, and are in good health. The completion of the questionnaire prior to the beginning the study will help minimize the risks of any cardiac event. Also, associated with an exercise test of this nature are leg and breathing discomfort (100%), as well as increases in body temperature (100%). If any adverse reactions occur due to exercise testing, you will be referred to your personal physician or the CSUS Student Health Center if you are a student. In case of severe or acute signs and symptoms we will follow CSUS Guidelines for Emergencies and when necessary Adult CPR/automated external defibrillator procedures.

**Benefits:** The benefits to yourself for participating in this study include knowledge of your maximal ability to consume oxygen, your maximal heart rate and your body’s metabolism. This information can be used to help optimize your training and understand your body’s response to exercise.

**Confidentiality:** If you decide to participate, you are free to withdraw your consent and to stop participation at any time with no penalty to you. Any information which is obtained in connection with this study and that can be identified with you will remain confidential and will be disclosed only with your permission. The data will be identified only with numeric codes, not the names of the participants

**Contact information:** If you have any questions, please feel free to call me, Roberto Quintana, PhD at (916)278-4495 between 9am and 5pm.

**Statement of Permission:** You are making a decision whether to participate or not participate. Your signature indicates that you have decided to participate having read the information provided. Your signature also affirms that the medical history you have provided is complete and true to the best of your knowledge. You will be given a copy of this form to keep.

__________________________  _________________________________
Date                        Signature of Participant

__________________________  _________________________________
Date                        Signature of Investigator
APPENDIX B

Subject Medical History and Questionnaire
SUBJECT INFORMATION AND MEDICAL HISTORY

NAME: ________________________________________________________________

DATE ________________________________

ADDRESS: ____________________________________________________________

PHONE: _______________________________

EMAIL: ______________________________

OCCUPATION: __________________________________________________________

GENDER: Female AGE ______ yrs DATE OF BIRTH _______________________

WEIGHT ______ kg HEIGHT ______ cm BP ______/____ mmHg

HR ______ beats/min TOTAL CHOLESTEROL ______ mg/dL HDL ______

mg/dL LDL ______ mg/dL TG ______ mg/dL

FASTING BLOOD GLUCOSE ______ mg/dL

Other blood results: ___________________________ This box is for personnel only

MEDICAL HISTORY: (Please Circle your Answer)

Are you currently taking any medications: Yes or No

If yes, please list: ____________________________________________________________________

Are you currently taking an oral contraceptive? YES or NO

If YES

Type (circle one): monophasic tiphasic other

EthinylesEstradiol (EE) Dose: ____________

ProGestogen (PG) Dose ____________

PG Type (circle 1) levonorgestrel norethindrone acetate desogestrel

norgestimate norgestrel etynodiol

How many consecutive months/years have you been taking your currently prescribed OC? ______

If NO

Are your monthly cycles regular (18-35 days apart and 3-8 day menses duration)? YES or NO

Have you ever taken an OC medication in the past? YES or NO

If YES How many months/years have you been off the medication? ____________

The date of your the last menstrual period was ____________ and number of periods over last year ______.
Please list all medical conditions (e.g. ulcers, arthritis, mono, hepatitis, HIV, musculoskeletal injury)?

Please list any hospitalizations and/or surgeries?

Have you ever been diagnosed with a breathing problem such as asthma? Yes or No.
If yes, please explain

Have you ever been diagnosed with a heart problem or condition? Yes or No.
If yes, please explain:

Do you have any of the following symptoms at rest or with low to moderate physical activity? Yes or No
Lightheadedness Shortness of Breath Chest Pain Numbness
Fatigue Coughing Wheezing Other
If yes, please explain:

Do you have any of following cardiovascular disease risk factors? Yes or No
Family History of Heart Attacks Hypertension
Sedentary Lifestyle High Cholesterol
Diabetes Current cigarette smoker Obesity
If yes, please explain:

Do you have an immediate family member with any of the following diseases? Yes or No
Diabetes Hypertension High Cholesterol Obesity
If yes, please explain:

Are there any other conditions that might affect your health/exercise ability such as liver or kidney disease? Yes or No:
If yes, please explain:

Physical Activity / Training History
Do you engage in regular physical activity – more than 30 minutes of physical activity at moderate intensity for at least 5 times a week? Yes or No: Please list mode/s of exercise:

What is/are the frequency/ies of your exercise session/s per week? (How many days a week)
What is/are the duration/s of your exercise session/s? (How long)
________________________________________________________________________

What is/are the intensity of your exercise bout/s? (How Hard)
________________________________________________________________________

What is the total volume of your workouts per week (miles per week)
________________________________________________________________________

How many years have you been physically active?
________________________________________________________________________

Have you ever performed a fitness or maximal exercise test? Yes or No:
If yes, what were the results of your tests?
ECG ________________ VO2 max ________________
Workload ______________ % BF ______________
Overall Interpretation:
________________________________________________________________________

**Competitors or Athletes**
Do you perform hard/high intensity intervals in your training or consider yourself a competitive athlete? Yes or No: If yes, please explain (list recent personal bests or awards)

Years/months of competitive cycling: _____________
 Discipline (circle all that apply): cross  MTB  road  track
APPENDIX C
Dietary and Physical Activity Log
Dietary & Physical Activity Log Recall

Please list all foods eaten the past 24 hours prior to today’s test and repeat this similar diet 24 hours prior to your next trial.

Dietary Recall:
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________

Physical Activity Recall:
List all physical activities and exercise that you participated in 24 hours prior to testing.
Please follow the same physical activities 24 hours prior to next test.
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
REFERENCES


