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Title: Hormonal Contraceptive Use Does Not Affect Strength, Endurance, or Body Composition Adaptations to Combined Strength and Endurance Training in Women

Year: 2021

Version: Accepted version (Final draft)

Please cite the original version:

Myllyaho, M., Ihalainen, J., Hackney, A., Valtonen, M., Nummela, A., Vaara, E., Häkkinen, K., Kyröläinen, H., & Taipale, R. (2021). Hormonal Contraceptive Use Does Not Affect Strength, Endurance, or Body Composition Adaptations to Combined Strength and Endurance Training in Women. Journal of Strength and Conditioning Research, 35(2), 449-457. https://doi.org/10.1519/JSC.0000000000002713

Journal of Strength and Conditioning Research

Hormonal contraceptive use does not affect strength, endurance or body composition adaptations to combined strength and endurance training in women

--Manuscript Draft--

Manuscript Number:	JSCR-08-10185R1
Full Title:	Hormonal contraceptive use does not affect strength, endurance or body composition adaptations to combined strength and endurance training in women
Short Title:	Hormonal contraceptive use in combined strength and endurance training
Article Type:	Original Research
Keywords:	combined strength and endurance training, hormonal adaptations, physical performance
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Manuscript Region of Origin:	FINLAND
Abstract:	This study examined the effects of a 10-week period of high intensity combined strength and endurance training on strength, endurance, body composition, and serum hormone concentrations in physically active women using hormonal contraceptives (HC, n = 9) compared to those who had never used hormonal contraceptives (NHC, n = 9). Training consisted of two strength training sessions, and two high-intensity running interval sessions per week. Maximal bilateral isometric leg press (Isom), maximal bilateral dynamic leg press (1RM), countermovement jump (CMJ), a 3000-m running test (3000m), body composition, and serum hormone levels were measured pre and post training between days 1- 5 of each subject's menstrual cycle. Both groups increased 1 RM and CMJ: HC = 13.2% ($p < 0.001$) and 9.6% ($p < 0.05$), and NHC = 8.3% ($p < 0.01$) and 8.5% ($p < 0.001$). HC improved 3000m by 3.5% ($p < 0.05$) and NHC by 1% (n.s.). NHC increased lean mass by 2.1% ($p < 0.001$) while a body fat percentage decreased from 23.9 ± 6.7 to 22.4 ± 6.0 (-6.0%, $p < 0.05$). No significant changes were observed in body composition in HC. No significant between-group differences were observed in any of the performance variables. LH concentrations decreased significantly ($p < 0.05$) over 10 weeks in NHC, while other hormone levels

	remained statistically unaltered in both groups. It appears that the present training is equally appropriate for improving strength, endurance, and body composition in women using HC as those not using HC without disrupting hypothalamic-pituitary-gonadal axis function.
Response to Reviewers:	RE: JSCR-08-10185, entitled "Hormonal contraceptive use does not affect strength, endurance or body composition adaptations to combined strength and endurance training in women" Dear Editor-in-Chief, We have revised our manuscript according to the requests and notes by the Editorial Board as well as reviewers #1 and #2. We hope that, these corrections adequately address your concerns and the present paper is now considered for publication. Below you will find detailed responses to the reviewer comments. 1. Make sure your human use informed consent is worded per author instructions and that if you include anyone who is under the age of 18 years of age, parental or guardian consent has been given and noted in this section. Please give the age range if your mean and SD suggest the subjects may have been under the age of 18 years. The age range of subjects (24–41 years) is given in the "Subjects" section, page 6, and in table 1. We have added the following sentence in the text under "Subjects": The methodology of the present study was approved by the Ethical Committee at the University of Jyväskylä. The chosen subjects were informed of the benefits and risks of the investigation prior to signing an institutionally approved informed consent document to participate in the study. 2. Make sure that your affiliation information or contact information for the corresponding author are on the title page of the paper as the title only page is used for the blinding; Contact information is only included on the title page, not in the manuscript. 3· Make SURE you have all your tables and figures attached and noted in the paper both text and where it should be placed. Our tables and figures are now attached and noted in the paper (in text and where they should be placed). Thank you for noticing this oversight on our part. 4· Very IMPORTANT ---Table files must be MADE in Word NOT copied into Word! Thank you for noticing, the tables are now made in Word, not copied into Word. 5. No PDFs submitted just Word and appropriate files e.g.,PPT for figures as a pdf will be built by EM at the end for your approval. Thank you, this has been noted. 6. Check all formatting and titling and make sure it is correct or this can delay publication in the process. Please read carefully the newest author instructions as well and comply. Formatting and titling should be in line with the instructions. 7. Make sure each table or figure is cited in the text and that it is part of the revision not just the original submission. Each table and figure is cited in the text. 8. If people are used in a figure not black eyes or face mask are allowed. No people are used in our figures. 9. Make sure your references are in proper format. End Note has our style for down load. Thank you for noticing this small mistake, we have made the correction (journal names in italics). Reviewer #1: Thank you for submitting your manuscript for consideration in The Journal of Strength and Conditioning Research. Introduction. The introduction is well written, defines the question about the use of synthetic contraceptive hormones during training programs in women. Can the authors describe additionally if there are phase effects in paragraph page 4. The literature cited notes the type of pill and outcome, but does not specify which part of the actual cycle tested or even if that is relevant? Did any of these studies compare to a control group not on synthetic hormones for a comparison to better understand the outcomes from a contraceptive perspective. In reading over the purpose statement and experimental approach section, there is emphasis of muscle hypertrophy and body composition changes. But there is missing a discussion about the body composition component from the Introduction. Please address. The author provide a clear purpose statement in the abstract----can this be done at the end of the last paragraph and possibly a

hypothesis as well.---this is done in the Experimental Approach---but move to Introduction. And then modify experimental approach section accordingly.

Thank you for your valuable comments. We have now specified the menstrual phase in literature cited, and added information about studies related to body composition. For example, Casazza et al. (2002) and Suh et al. (2003) demonstrated that 4 months of a low-dose, triphasic hormonal contraceptive use significantly increased body weight and fat mass in moderately physically active young women. Similarly, Lebrun et al. (2003) reported in a double blind, placebo controlled trial that a significant increase was observed in the sum of skinfolds in women taking triphasic hormonal contraceptives compared with those taking placebo. In addition, we have moved the purpose statement and hypothesis from Experimental Approach to Introduction, as suggested. We have also modified the wording of the Experimental Approach, as suggested. All changes are marked in red in the manuscript.
Methods-
1.Subjects-- Why was the resting EKG necessary---please address here.

Thank you for noticing. All subject candidates completed a health questionnaire and a resting ECG screening that were reviewed by a physician before inclusion in the study. This was done in order to exclude any diseases, musculoskeletal or cardiac problems, or medications that would preclude a subject's ability to perform resistance and endurance training and testing as per standard procedure in our laboratory. Any abnormalities in resting ECG were to be addressed by a physician (cardiologist). Fortunately, no abnormalities were observed in this subject population. This is also clarified in the Methods (page 6).

2.The discussion indicated that all women were on monophasic pills---at what doses? were these similar? could it have affected outcomes?

Thank you for this important question. We have added dosages to the "Experimental Approach to the Problem" (page 5) as follows: Hormonal contraception used by the subjects consisted of monophasic combined pills (0.02–0.035 mg ethinyloestradiol and progestins in different doses; 3 mg drospirenone, 0.075 mg gestodene or 0.150 mg desogestrel), progesterone-only pills (0.35 mg norethisterone or 0.075 mg desogestrel), and intrauterine systems (levonorgestrel 13–52 mg), all of which are frequently prescribed clinically (11).
It is possible that different dosages could affect outcomes but, however, we did not want to single out a specific dosage at this point in our research. The effect of different dosages currently goes beyond the scope of this manuscript.

3.Study Design and Training-Regarding control factors---were subjects allowed to do any other activities outside of the training program.?--although this was eluded to in the discussion-- Were the 1RM re-tested halfway through the ensure that 85% of 1RM was still 85% if subjects were to get stronger over time. How was HRmax determined? VO2 max test or Karvonen formula or other method? The training program does not indicate any rest periods between sets and different exercises? Were the exercises always completed in the order that is listed in this section or random?

Thank you for this comment. We have added the details requested.
Subjects were allowed to continue with other habitual physical activities during the study to ensure that overall training volume did not decrease. In addition, the subjects were given instructions and support to ensure that the present intervention would be performed with high quality.
All subjects participated in pre-, mid- and post-measurements, but mid-measurements are not reported in this study. Unfortunately, mid-measurements only consisted of a lower number of neuromuscular measurements (countermovement jump and isometric leg press), and not dynamic leg press, so 1RM was not re-tested halfway. Strength training sessions were, however, closely monitored by experienced trainers to help ensure that loads were properly increased to maintain an adequate training stimulus in terms or repetitions per set (the final repetition should require full effort/achieve failure. HRmax was determined using an incremental running test until exhaustion on a treadmill before the intervention. In the treadmill test, the incline remained a constant 1-degree throughout the test, but the running velocity began at 7−9 km·h-1 and was increased by 1 km·h-1 every third minute until volitional exhaustion. Heart rate was

monitored using a heart rate monitor (Suunto t6, Vantaa, Finland).
Our training section has been updated as follows: The main exercises included maximal and explosive sets of squat, bilateral leg press, knee flexion, calf raise and calf jump (2–3 sets/movement, 6–10 repetitions/set, 1–2 min recovery between sets and exercises). The main exercises were followed by explosive sets of plyometric exercises without external load: drop jumps, plyometric strides, step-ups and hurdle-jumps (2 sets/movement, 6–10 repetitions/set, rest intervals were two minutes at the beginning of the study, and were reduced to one minute during the training period), and core exercises (6 sets, 10–15 repetitions/set, 1 min rest intervals). For the main exercise,s there was no exercise order. However, contrast movements were always performed after the biomechanically similar heavier movement. Strength training sessions were performed in a gym that was built for research purposes and supervised by members of research staff. All performed sets, reps and loads were recorded in individual training diaries.

4.Was training AND data collection always done at the same time of day?

Thank you for this question. The measurements were done at the same time of day (±2 hours) for each subject to control for circadian variations. We have added this information to “Data collection and Analysis” (page 8):
In addition, we have added information to “Study Design and Training” (pages 7-8): Subjects were allowed to train strength and endurance sessions in which order they preferred, but two same training modalities were not allowed subsequent days. In addition, subjects were informed not to complete four training sessions in a row, recommendation being two training days in a row continued with a rest day. Training was completed at the same time of day with a few minor exceptions.
5.Was a history taken of the menstrual cycle to know that the cycle was consistent, even on contraceptives?

Thank you for this comment. A regular menstrual cycle was mentioned during recruitment of subjects and for this study was self-reported by each subject. We have added the following information to “Subjects“section (page 6): All subjects in both groups reported regular menstrual cycles (24–35 days).
6.Anthropometric Measures
When author state 'underwear' does this mean undergarments in general? Typically a gown or other clothing is allowed and not just in undergarments? Please address. Define how height and weight were taken---digital scale, etc to nearest 0.5 kg, etc???? need manufacturer, city, etc for ht and wt equipment. Did the DXA scan look at regional body composition.
Thank you for your comment. The subjects were indeed just in their undergarments. This is standard procedure in our lab. We have added the following information to the manuscript: Height was measured using standard methods to an accuracy of 0.5-cm. Body weight was measured in conjunction with dual-energy x-ray absorptiometry (DXA) measurements (Lunar Prodigy Advance, GE Medical Systems – Lunar, Madison WI USA) to an accuracy of 0.1kg.
The system software for DXA automatically provided the mass of lean soft tissue, fat, fat free mass, and bone minerals for the whole body and specific regions (trunk, upper body, lower body), the results for upper body and lower body were similar with the changes in whole body and thus only whole-body values were reported.

7.Strength
It is curious to know about just lower body--body composition changes since the majority of exercises were of the lower body in addition to the total % body fat, etc.

The changes in lower body fat-% (4.8% in NHC and 4.1% in HC) and lean mass (4% in NHC and 0.9% in HC) were similar magnitude with the changes in total fat-% and total lean mass. For the purpose of this publication we report lower body composition. Another manuscript that is in preparation reports whole body changes.

8.Endurance
Was HR taken during the 3000m test to get an indication of intensity?
HR was measured during the 3000m running test to monitor intensity, however, we do not report this in the manuscript.

9.Blood
What amount was drawn in total? Were samples run in duplicate?
We have added the blood draw amount (4.0 ml) in our revised manuscript. The samples were not run in duplicate.

10.Graphs-Please format appropriately such that the figure with the figure headers are placed at the end of the file near the tables. Typically the vertical axis has the variables name and units listed on the actual axis, inverted.
We have completed these revisions as suggested.

11.Tables--typically for JSCR the table significant symbols definitions go under the table and not together with the title of the table.
Thank you for noticing, we have made the correction in the tables as suggested.

12.Results-please explain effect size outcomes in writing.
Thank you for this comment. We have included explanations of effect size in our discussion.

13.Discussion--Did the authors think that a significant change in body comp (BMI, body fat) was going to occur in this population? The BMI was 21 on average and the fat% was 23%---moderate levels for this age group. Possible if BMI and BF% were higher greater changes might have been seen??? Can this be addressed?

Thank you for your comment. It is likely that a higher BMI and BF% for the target population would have yielded greater changes than what were noted in the present study. However, there does not appear to exist literature to confirm this using a similar study design. We hypothesized that significant changes in body composition (increased lean mass and decreased fat%) would occur, however, based on previous research of combined strength and endurance training conducted on both men and women (Mikkola et al. 2011, Sillanpää et al. 2010, Taipale et al. 2014). In addition, by reflecting on other literature including the study of Lebrun et al. 2003 in which there was a significant increase in fat% after OC use in highly trained athletes with initial fat% of only 17 on average. Similarly, in the study of Suh et al. 2003 the fat% was increased significantly after OC use in subjects with similar fat% and BMI that in our study.

14.Good explanation about the blood variable in terms of physiological reasons. For conclusions---could it be stated that the hormonal contraceptives----given the dose that were used----does not have impact on LBm and BF%???? Also the effect sizes are not discussed in either results or discussion--please address.

Thank you for this comment. We agree that the conclusion should have mention of the dosage and we have modified the “Conclusion” as follows (page 19): In addition, it appears that use of low dose monophasic hormonal contraceptives does not have a significant negative impact on development of lean mass and reduction of fat% due to exercise training.
Discussion of effect size is also now included.
15.Ref--note that the journal names need to be in italics
Thank you for noticing our mistake, we have made the correction as suggested.

Reviewer #2: Very good study - I only have a few comments.
1. More information should be given regarding the training status of the subjects prior to initiating the study, i.e. familiar with RT? How many months/years?
Thank you for this comment, we have addressed this under the heading “Subjects” (page 6): Training background of the subjects consisted of different endurance activities such as jogging, orienteering, and cross-country skiing. Elite athletes were not included in the study. None of the subjects had participated in strength training regularly before the intervention.

2. Figure 1 and legend should not be embedded within the text
Thank you for noticing this mistake. In the revised manuscript, we have corrected it accordingly.

Journal of Strength and Conditioning Research

Hormonal contraceptive use does not affect strength, endurance or body composition adaptations to combined strength and endurance training in women

Running head: Hormonal contraceptive use in combined strength and endurance training

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Hormonal contraceptive use does not affect strength, endurance or body composition adaptations to combined strength and endurance training in women

Running head: Hormonal contraceptive use in combined strength and endurance training

ABSTRACT

This study examined the effects of a 10-week period of high intensity combined strength and endurance training on strength, endurance, body composition, and serum hormone concentrations in physically active women using hormonal contraceptives (HC, n = 9) compared to those who had never used hormonal contraceptives (NHC, n = 9). Training consisted of two strength training sessions, and two high-intensity running interval sessions per week. Maximal bilateral isometric leg press (Isom), maximal bilateral dynamic leg press (1RM), countermovement jump (CMJ), a 3000-m running test (3000m), body composition, and serum hormone levels were measured pre and post training between days 1−5 of each subject's menstrual cycle. Both groups increased 1 RM and CMJ: HC = 13.2% ($p < 0.001$) and 9.6% ($p < 0.05$), and NHC = 8.3% ($p < 0.01$) and 8.5% ($p < 0.001$). HC improved 3000m by 3.5% ($p < 0.05$) and NHC by 1% (n.s.). NHC increased lean mass by 2.1% ($p < 0.001$) while a body fat percentage decreased from 23.9 ± 6.7 to 22.4 ± 6.0 (-6.0%, $p < 0.05$). No significant changes were observed in body composition in HC. No significant between-group differences were observed in any of the performance variables. LH concentrations decreased significantly ($p < 0.05$) over 10 weeks in NHC, while other hormone levels remained statistically unaltered in both groups. It appears that the present training is equally appropriate for improving strength, endurance, and body composition in women using HC as those not using HC without disrupting hypothalamic-pituitary-gonadal axis function.

Key words: combined strength and endurance training, hormonal adaptations, physical performance

INTRODUCTION

The effects of combined strength and endurance training on health and performance have been of great interest to researchers in past years, but research has most often been conducted with male subjects (9, 10). Female physiology is complicated with changing levels of endogenous sex hormones across the menstrual cycle, which may also be modified by exogenous sex hormones introduced into the body by a way of hormonal contraceptives. Hormonal contraceptives are commonly prescribed to both non-athletes and athletes for purposes such as contraception, cycle regulation, treatment of amenorrhea and painful menstruation, as well as for the maintenance of bone density (12, 29). Overall, exposure to estrogens during different phases of life has long-term effects on a woman's health and wellbeing (33) while alterations in these sex hormones may have an effect on cardiovascular function (25, 26), thermoregulation(20, 26), and substrate metabolism(1, 6, 15, 27, 36).

Exogenous female sex hormones in hormonal contraception systematically controls the concentrations of endogenous sex hormones in a woman's body by acting on the hypothalamus and anterior pituitary glands leads to the suppression of gonadotropin-releasing hormone (GnRH), follicle stimulating hormone (FSH), and luteinizing hormone (LH) thus, suppressing endogenous estrogens and progestins. Depending on the type of hormonal contraception administered, 3–5 times more exogenous estrogen and 1–3 times more exogenous progesterone than endogenous levels can be provided(4, 14). Hormonal contraceptives reduce the levels of total and free testosterone by inhibiting ovarian and adrenal androgen synthesis and by increasing levels of sex hormone-binding globulin (SHBG) (29, 37, 39). Despite the widespread use of hormonal contraceptives, little is known about the effects of synthetic female sex hormones used in hormonal contraceptives on adaptations to training(6).

Studies with monophasic and triphasic combination pills suggest that hormonal contraceptive use does not affect maximal muscular force production(14, 30) or isokinetic strength (23). Studies reporting changes in endurance performance and body composition are equivocal. In general, studies that involve low dose-, monophasic-, combination pills suggests that hormonal contraceptive use does not affect endurance performance or body composition of regularly menstruating active women during the early-follicular phase (22) in either athletes or sedentary controls with regular menstruation (22, 29). However, there are reports of reduced maximal oxygen consumption (VO_{2max}) and increased total body fat associated with the use of triphasic hormonal contraceptives, studied in both the early-follicular and mid-luteal phases of an ovulatory menstrual cycle in both moderately active women (5, 34) and highly trained endurance athletes (23). For example, Casazza et al. (2002) and Suh et al. (2003) demonstrated that 4 months of a low-dose, triphasic hormonal contraceptive use significantly increased body weight and fat mass in moderately physically active young women (5, 34). Similarly, Lebrun et al. (2003) reported in a double blind, placebo controlled trial a significant increase in the sum of skinfolds in women taking triphasic hormonal contraceptive compared with those taking placebo (23). In fact, it seems that triphasic formulations with higher progestrogenic and androgenic activity may have more pronounced negative effects on endurance performance and body composition in the short term compared with formulations with lower potency and androgenicity (4, 5, 34). It is difficult to interpret these opposing findings because of the differences in menstrual history, hormonal contraception formulations, and duration of use between subjects and between studies, as well as variations in experimental design. The aim of this study was to clarify this issue by examining how non-specified monophasic hormonal contraceptive use affects strength, endurance, and body composition adaptations to 10 weeks of high-intensity combined strength and endurance training performed on separate days in physically active women. We hypothesize that hormonal contraceptive use may blunt

improvements in strength and endurance performance and may even slightly inhibit muscle hypertrophy and fat loss over the present 10-week training period.

METHODS

Experimental Approach to the Problem

To investigate the effect of hormonal contraceptive (HC) use on strength and endurance training, one group of women using HC and another group of normally menstruating women, who were not using HC (NHC group), completed the study protocol. Measurements were completed during each subject's self-reported follicular phase before and after 10 weeks of high-intensity combined strength and endurance training. Maximal bilateral isometric leg press (Isom), maximal bilateral dynamic leg press (1RM), counter movement jump (CMJ), a 3000-m running test (3000m), body composition, and serum hormone levels were measured pre and post training and compared between the groups. Hormonal contraception used by the subjects consisted of monophasic combined pills (0.02–0.035 mg ethinyloestradiol and progestins in different doses; 3 mg drospirenone, 0.075 mg gestodene or 0.150 mg desogestrel), progesterone-only pills (0.35 mg norethisterone or 0.075 mg desogestrel), and intrauterine systems (levonorgestrel 13–52 mg), all of which are frequently prescribed clinically (11).

******Table 1 approximately here******

Subjects

A total of 18 healthy, physically active women (age 24–41 years) were recruited to participate in this study (Table 1). The study group included nine women who had at least one year of hormonal contraceptive use (HC: n = 9), and nine women who had never used hormonal

contraceptives (NHC: n = 9). All subjects in both groups reported regular menstrual cycles (24–35 days). Exclusion criteria included: body mass index > 30 kg/m^2, a Cooper running test result < 2300 m, illness, disease, injury or use of medications that would contraindicate participation in the study. All subject candidates completed a health questionnaire and a resting ECG screening that were reviewed by a physician before inclusion in the study, in order to exclude any diseases, musculoskeletal or cardiac problems, that would preclude a subject's ability to perform resistance and endurance training and testing. Training background of the subjects consisted of different endurance activities such as jogging, orienteering, and cross-country skiing. Elite athletes were not included in the study. None of the subjects had participated in regular strength training prior to the intervention. The methodology of the present study was approved by the Ethical Committee at the University of Jyväskylä. The chosen subjects were informed of the benefits and risks of the investigation prior to signing an institutionally approved informed consent document to participate in the study.

Procedures

Study Design and Training

The subjects were examined before and after 10 weeks of high-intensity combined strength and endurance training. A total of four high intensity training sessions per week was performed by each subject and consisted of two strength training sessions and two running interval training sessions. The strength training was targeted at the lower extremities. Every strength training session consisted of several multi-joint movements with progressively increasing loads from 50 to 85% 1 RM during the training period. The main exercises included maximal and explosive sets of squat, bilateral leg press, knee flexion, calf raise and calf jump (2–3 sets/movement, 6–10 repetitions/set, 1–2 min recovery between sets and exercises). The main exercises were followed by explosive sets of plyometric exercises without external load: drop

jumps, plyometric strides, step-ups and hurdle-jumps (2 sets/movement, 6–10 repetitions/set, rest intervals were two minutes at the beginning of the study, and were reduced to one minute during the training period), and core exercises (6 sets, 10–15 repetitions/set, 1 min rest intervals). For the main exercises there was no specified exercise order, however, contrast movements were always performed after the biomechanically similar heavier movement. Strength training sessions were performed in a gym that was built for research purposes and supervised by members of research staff. All performed sets, reps and loads were recorded in individual training diaries.

Endurance training sessions consisted of one high-intensity interval training session with 4x4 min running intervals progressing in intensity from +70% maximal heart rate (HR_{max}) to 90% of HR_{max} over the course of the 10-week training period (4 min rest with 60−70% HR_{max}), and one sprint training session with 3x3x100 m all-out sprints (2 min rest with 60−70% HR_{max}/ 5 min between sets) per week. The heart rate (HR) values were recorded and collected before and after every interval, and thus used as a way to monitor training intensity. HR_{max} was determined in an incremental running test to exhaustion on a treadmill before the intervention. In the treadmill test the incline remained a constant 1-degree throughout the test. Running velocity began at 7−9 $km \cdot h^{-1}$ and was increased by 1 $km \cdot h^{-1}$ every third minute until volitional exhaustion. Heart rate was monitored using a heart rate monitor (Suunto t6, Vantaa, Finland).

Subjects were allowed to train strength and endurance sessions in the order in which they preferred, however, two same training modalities were not allowed subsequent days. In addition, subjects were informed not to complete four training sessions in a row, the recommendation being two training days in a row followed by a rest day. Subjects were allowed to continue with other habitual physical activities during the study to ensure that overall training volume did not decrease. In addition, the subjects were given instructions and support

to ensure that the present intervention would be performed with high quality. In addition, it was recommended that subjects complete one higher-volume (≥ 2 hour) low-intensity aerobic exercise every week. All training was completed at the same time of day with a few minor exceptions.

Data Collection and Analysis

The subjects were instructed to schedule the PRE- and POST-measurements at the beginning of their menstrual cycle during the follicular phase between days 1−5. Data collection consisted of anthropometric measurements (dual-energy x-ray absorptiometry), strength performance measurements (isometric and dynamic leg press, countermovement jump), cardiorespiratory performance measurements (3000-m time trial), and collection of blood samples for determination of resting levels of serum hormones. The measurements were done at the same time of day (±2 hours) for each subject to control for circadian variations.

Anthropometric Measurements

Anthropometric measurements were completed in a fasted (12 h) state with subjects wearing only their undergarments. Height was measured using standard methods to an accuracy of 0.5 cm. Weight was measured in conjunction with dual-energy x-ray absorptiometry (DXA) measurements (Lunar Prodigy Advance, GE Medical Systems – Lunar, Madison WI USA) to an accuracy of 0.1 kg. In addition, estimates of muscle and fat tissues were measured using dual-energy x-ray absorptiometry (DXA). At the beginning of the measurements, the subject was positioned supine in the center of the DXA table with their arms at their sides and feet

together. The subject was scanned using the default scan mode for total body scanning automatically selected by the Prodigy software (enCORE 2005, version 9.30 and Advance 12.30). The system software provided calculations of body fat% and lean mass for analysis.

Strength Performance

Isometric strength of the leg extensor muscles was measured using an electromechanical isometric bilateral leg extension device (Designed and manufactured by Biology of Physical Activity, University of Jyväskylä, Finland). Subjects were instructed to exert their maximal force as fast as possible during a period of approximately 3 s in a sitting horizontal position with the knee angle of 107°. They performed at least three maximal voluntary contractions. The best performance trial, in terms of maximal force, was used for statistical analysis. Force data was collected at a sampling frequency of 2000 Hz, and then filtered (20 Hz low pass filter) and analyzed using customized scripts (Signal 4.04, CED, UK).

Maximal bilateral dynamic concentric strength was estimated with one repetition maximum (1RM) of leg press in a horizontal sitting position (David Sports Ltd., Helsinki, Finland). After sub-maximal warm-up sets with increasing weight and decreasing repetitions: 5 x ~70% 1RM, 2 x ~80–85% 1RM and 1 x ~90–95% of estimated 1RM (with one minute of rest between sets), the greatest weight, with the accuracy of 1.25 kg, that the subject could successfully lift was determined as 1RM. The action started from a knee angle of approximately 60º, and legs were extended to a full range of motion (180º). Subjects were instructed not to lock their knee joints at full extension, and to keep constant contact with the seat and backrest during leg extension. Verbal encouragement was provided.

Dynamic explosive force characteristics of the leg muscles were measured on a force platform by using countermovement jump (CMJ). Subjects were instructed to jump as high as possible with an explosive countermovement action before the concentric phase of the movement. The hands were kept on the hips during the jump. Subjects performed three jumps with one minute rests between. The jump height was calculated from the flight time (Signal 4.10, CED, UK).

Endurance Performance

A 3000-m time trial was performed on a 200-m indoor track. After a 10-min warm-up at self-determined intensity, subjects were verbally encouraged to run 3000 m as fast as they could. Split times for each kilometer were recorded and the final time in seconds (s) was used for analysis. HR was recorded after each 200-m lap to monitor intensity.

Blood Samples and Serum Hormones

Venous blood samples (4.0 ml) were collected from participants in a fasted state (12 h), using sterile needles into serum tubes (Venosafe, Terumo Medical Co., Leuven, Belgium) by a qualified lab technician. Whole blood was spun for 10 minutes at 2500 rpm (Megafuge 1.0R, Heraeus, Germany). Serum samples were frozen at -80ºC until analysis. Blood samples were collected for the determination of serum concentrations of total testosterone (TT), FSH, LH, estradiol (E), progesterone (P), SHBG, cortisol (C), and insulin-like growth-factor I (IGF-I). Serum samples were analyzed using chemical luminescence techniques (Immulite 2000 XPi, Siemens, Llanberis, UK) and hormone specific immunoassay kits (Siemens, New York, NY,

USA). The sensitivity for TT, FSH, LH, E, P, SHBG, C, and IGF-I were 0.5 nmol/l, 0.1 mIU/ml, 0.1 mIU/l, 55 pmol/l, 0.1 ng/ml, 0.2 nmol/l, 5.5 nmol/l, and 0.26 nmol/l, respectively. The inter assay coefficients of variation for TT, FSH, LH, E, P, SHBG, C, and IGF-I were 9.4%, 6.0%, 7.8%, 12.0%, 8.5%, 5.4%, 6.6%, and 6.4%, respectively.

Statistical Analysis

All data was analyzed and graphed using Microsoft Excel 2010 and IBM SPSS Statistics v.20 computer software. Conventional statistical methods were used for the calculation of means and standard deviations. Before applying further statistical methods, the data was checked for normality. The data was normally distributed in performance variables and in body composition variables. Non-parametric Wilcoxon and Mann–Whitney tests were used when a specific variable violated the assumptions of parametric tests. Independent-samples' T-test was used for analyzing between group differences in separate timepoints. A repeated ANOVA with two levels (PRE, POST) was used for analyzing within group differences at different time points. The significance for all tests was set at * = $p < 0.05$, ** = $p < 0.01$ and *** = $p < 0.001$. Effect sizes (ES) are expressed using Cohen's d. When $d \geq 0.20$ effect size was considered to be small, when $d \geq 0.50$ effect size was considered to be medium, and when $d \geq 0.80$ effect size was considered to be large (8).

RESULTS

There were no significant differences in any performance variables between HC and NHC before the training period. Strength adaptations were similar in both groups, and there were no

statistically significant differences in the increases between the groups. Maximal isometric leg press force, 1 RM in dynamic leg press and countermovement jump increased in the HC group by 18.6 ± 11.0% ($p < 0.01$), 13.2 ± 7.2% ($p < 0.001$), and 9.6 ± 8.7% ($p < 0.05$), respectively, and in the NHC group by 6.8 ± 12.2% (n.s.), 8.3 ± 6.6% ($p < 0.01$) and 8.5 ± 6.3% ($p < 0.001$), respectively.

The HC group improved their running time by 3.5 ± 4.5% ($p < 0.05$) and NHC group by 1.0 ± 3.3% (n.s.). The improvement of the 3000-m time trial was significant only for the hormonal contraception group, but no significant difference between the groups was observed. All the strength and endurance characteristics before and after the 10-week training period are presented in Table 2 along with effect sizes.

******Table 2 approximately here******

The NHC group had a significant increase in lean body mass by 2.1 ± 1.0% ($p < 0.001$). In the HC group, lean mass was not increased significantly (1.0 ± 1.6%, n.s., $d = 0.82$ large). Fat% was not reduced significantly in the HC group (-6.3 ± 8.8%, n.s.), whereas in the NHC group, body fat percentage decreased from 23.9 ± 6.7 to 22.4 ± 6.0 (-6.0 ± 5.5%, $p < 0.05$, $d = 0.04$ small) (Figure 1).

******Figure 1 approximately here******

A significant group-time interaction in LH concentration was observed in the NHC group, LH decreased significantly ($p < 0.05$) from the PRE- to POST-measurements. In addition, a between-group difference in LH-levels was observed prior to the intervention with higher concentrations of LH in the NHC group than in the HC group ($p < 0.05$). Following the training period, estrogen-levels were significantly higher in the NHC group compared to the HC group ($p < 0.001$). A slight difference between the PRE-values of SHBG was observed with higher concentrations of SHBG in HC than in NHC ($p = 0.063$). No other significant changes in hormonal concentrations were observed from PRE to POST or between the groups in any of

the serum hormone concentrations measured. All serum hormone concentrations are presented in Table 3 along with effect sizes.

******Table 3 approximately here******

DISCUSSION

The main findings of the study were that strength and endurance performance improved similarly in both HC and NHC women over the 10-week combined strength and endurance training period, while no statistically significant differences in body composition changes were observed between the HC and NHC groups. In terms of serum hormone concentrations, TT, FSH, E, P, C, and IGF-I remained statistically unaltered from PRE to POST, while a significant decrease in LH concentrations were observed in the NHC group from PRE to POST. To our knowledge, this is the first published report investigating the effects of hormonal contraceptives on the mixture of strength, endurance, and body composition adaptations following combined strength and endurance training that also controls for menstrual cycle phase.

Strength (maximal bilateral isometric leg press force, 1RM, and countermovement jump height) and endurance performance (3000-m running time trial) improved similarly in both HC and NHC. Several published studies support the finding that hormonal contraceptive use does not affect baseline maximal force production (14, 23, 30) while the present results suggest that they do not seem to affect strength or power development either during the present 10-week combined endurance and strength training period

High-intensity interval training has shown to increase maximal oxygen consumption (VO_{2max}), muscle buffering capacity, time to fatigue, and, therefore, time trial performance (13, 19).

However, combining maximal and explosive strength and high-intensity endurance and sprint training did not significantly improve the time trial performance in the whole study group. When comparing the adaptations in endurance performance between the groups, the within group difference in 3000-m time trial was significant only in the HC group, although both groups improved their running time and no significant difference between groups' improvements was observed. Hormonal contraceptives did not impair adaptations in endurance performance. All the combined pills used in the present study were monophasic, and the results are in accordance with other studies examining monophasic pill-users and non-users in the early follicular phase (menstrual cycle days 1–5) that suggest that hormonal contraceptive use does not affect endurance capacity (22, 29).

When comparing the adaptations of body composition (lean mass and body fat%) between the groups, there were no statistically significant differences between HC and NHC, although interestingly, the NHC group concurrently showed a statistically significant increase in lean mass and a decrease in fat%. Previous research of combined strength and endurance training conducted on both men and women suggests that this type of training increases lean mass and decreases fat% (24, 31, 32, 35). Without a control group, it is not possible to know whether or not strength and muscle mass development was blunted by concurrently performing endurance activities, as observed in some other studies(3, 7, 18, 21, 38), especially during longer training interventions, when compared to the present 10-week period. The current subjects were asked to abstain from adopting any new diets or lifestyle changes during the study, and thus dietary conditions are assumed to have remained constant. In the literature, there are no similar experimental study designs as in the present study, but some studies with triphasic hormonal contraceptives have reported increased fat mass in moderately active women (6, 23, 34) as well

as female endurance athletes (23). It seems that the results may depend on the use of different types and formulations of hormonal contraception, since the potency and androgenicity of the progesterone within the hormonal contraception pill may play a significant role metabolically (4, 5, 34). In addition, increases in body mass and body fat usually occur within the first months of hormonal contraception use (4, 23, 34). In the present study, all subjects had at least one year of hormonal contraceptive use thus, changes in body composition cannot be attributed starting hormonal contraceptive use.

In the present study, concentrations of several hormones were examined in order to gain insights into the potential underlying mechanisms that may affect the physical performance adaptations in women with different sex hormone status. TT, FSH, P, C, and IGF-I remained statistically unaltered from PRE to POST. Nevertheless, LH levels at PRE were significantly higher in the NHC group compared to HC group, which can be explained by the suppressing actions of synthetic ovarian hormones on the hypothalamus and anterior pituitary gland. Synthetic ovarian hormones may even increase levels of sex hormone-binding globulin (SHBG), and reduce concentrations of bioavailable total and free testosterone (2, 4, 6, 14, 29, 37, 39). SHBG and TT levels were within normal ranges among HC users, although a slight but statistically insignificant difference between PRE-values of SHBG was observed with higher concentrations of SHBG in HC than in NHC. Interestingly, the E levels at POST were significantly higher in NHC compared to HC, although it is unclear why E concentration has increased. The lack of changes in P levels indicates that E production has not increased, hence, this E observation warrants further investigation.

The stability of serum concentrations of TT and C over the training period indicate maintained homeostatic control(9, 24, 35). Baseline serum TT levels may be an important indicator of trainability during strength training in terms of maximal strength and power development in women (16, 17). However, in the present study no differences were observed between the groups in the baseline TT levels and our subjects used a combined endurance and strength protocol throughout the 10-week training period. In addition, it must be taken into account that the individual variations in the TT levels in women are large, and increases in strength and muscle mass do not always coincide with increases in TT levels (9). Progesterone levels were similar in HC and NHC throughout the training intervention. Progesterone is reported to affect muscle force production, body composition, thermoregulation, and hemodynamics, as well as oppose the lipolytic effects of estrogen (1, 4, 5, 20, 26, 30, 34). Thus, stability in this hormone in both groups together with similar changes in the measured variables appear to be logical. Collectively, these hormone results indicate that the hypothalamic-pituitary-gonadal axis in the NHC group is functioning properly, which indicates that the present high-intensity training led to fitness improvements in these eumenorrheaic women without disrupting the hypothalamic-pituitary-gonadal axis. Similarly, the present training stimulus had no effect on hormonal concentrations of those women using hormonal contraceptives to regulate their menstrual cycle.

A strength of this study was the homogeneous nature of the groups in terms of performance variables and body composition, although the sample size was indeed rather small (HC: n = 9, NHC: n = 9). Some additional weaknesses in the study include that the subjects were instructed to schedule the PRE- and POST-measurements at the beginning of their menstrual cycle, between days 1−5. As this was self-reported, there is certainly some room for judgement error

by the subjects, particularly in the NHC group where more variation in cycle length can be expected. Our results do indeed suggest that some subjects were well into the follicular phase when samples were collected. It should also be kept in mind that the hormonal contraception formulations used in this study consisted of three different types; combined pills, progesterone-only pills, and intrauterine (hormonal) systems, which all have different active ingredients and number of exogenous hormones. Although all of these formulations were monophasic, the impact of different formulations on performance or training induced adaptations may vary, thus it is not possible to determine the exact effects of a specific formulations on performance. The purpose of this study, however, was to examine the general effects of hormonal contraception on a 10-week combined strength and endurance training period rather than to single out a specific oral contraceptive formulation. Future research, however, should consider this possibility.

Using Cohen's d to examine the magnitude of difference between groups suggests some medium and large differences between HC and NHC in strength (maximal bilateral isometric strength and 1RM), endurance (3000m running time trial), body composition (lean mass), and even hormones (FSH, LH and SHBG). These differences could suggest advantages/disadvantages of using hormonal contraceptives in terms of training adaptations, however, practically speaking; no clear advantage or disadvantage can be interpreted. While effect sizes appeared to favor the HC group in terms of performance variables, effect sizes appeared to favor the NHC group in terms of body composition. If these effect sizes are adjusted for exercise professionals as recommended by Rhea 2004 (28), however, the magnitude of difference between groups in terms of performance and body composition is small at best. Thus, further investigation is needed.

CONCLUSION

The findings of this study suggest that use of low-dose monophasic hormonal contraception does not affect strength or endurance performance adaptations to 10 weeks of combined strength and endurance training in physically active women when menstrual cycle was controlled for by completing measurements always at days 1-5 of the cycle. In addition, it appears that use of hormonal contraceptives does not have a significant negative impact on development of lean mass and reduction of fat% due to exercise training. Further investigation of strength, endurance, and body composition adaptations over longer training interventions in women using hormonal contraceptives is nonetheless still warranted.

PRACTICAL APPLICATIONS

The present 10 weeks of high-intensity combined strength and endurance training led to improvements in both strength and endurance of eumenorrheaic women not using hormonal contraceptives without disrupting the hypothalamic-pituitary-gonadal axis. Similarly, the present training stimulus led to improvements in both strength and endurance of women using hormonal contraceptives to regulate their menstrual cycle without having negative effects on hormonal concentrations. It appears that a 10-week block of combined high-intensity strength and endurance training is equally appropriate for improving strength, endurance, and body composition in women using hormonal contraceptives as those who have never used hormonal contraceptives.

Acknowledgments

The present study was part of a larger research project (VoKe project) which was carried out at Biology of Physical Activity, Faculty of Sport and Health Sciences, University of Jyväskylä. We thank the subjects for participating in this study, and the technical staff of Biology of Physical Activity, Faculty of Sport and Health Sciences, who provided much of the laboratory support throughout the study. We thank the Finnish Cultural Fund and Biology of Physical Activity, Faculty of Sport and Health Sciences, for financial support of this project.

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Figure

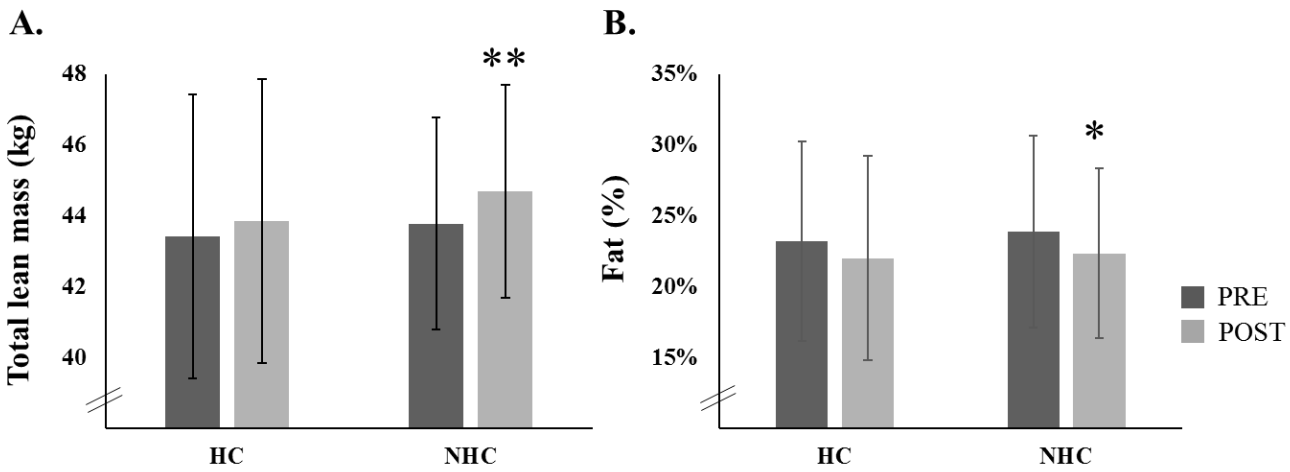

Figure 1. Mean (±SD) total lean mass (A) and fat% (B) before and after the training period. * = $p < 0.05$, and ** = $p < 0.01$.

Table

TABLE 1. Subject characteristics of hormonal contraceptive group (HC) and non-hormonal contraceptive group (NHC).

Group	n	Age (years)	Height (cm)	Body mass (kg)	BMI (kg/m^2)	Body fat (%)
HC	9	28.2 ± 3.1	166.4 ± 5.0	59.3 ± 5.3	21.4 ± 1.8	23.2 ± 7.1
NHC	9	31.3 ± 5.4	168.3 ± 5.0	60.6 ± 5.8	21.4 ± 1.7	23.9 ± 6.7

TABLE 2. Strength and endurance characteristics of the hormonal contraception (HC, n = 9) and non-hormonal contraception groups (NHC, n = 9) before (PRE) and after (POST) the 10-week training period.

	HC			NHC			Effect Size
Variables	**PRE**	**POST**	**Δ%**	**PRE**	**POST**	**Δ%**	**Cohen's d**
Isometric leg press force (N)	2840 ± 405	3270 ± 670**	18.6 ± 11.0	2680 ± 631	2810 ± 577	6.8 ± 12.2	d = 1.02 large
Dynamic leg press 1 RM (kg)	114 ± 15	124 ± 16***	13.2 ± 7.2	118 ± 18	128 ± 21**	8.3 ± 6.6	d = 0.71 medium
CMJ (cm)	25.8 ± 3.0	27.1 ± 4.2*	9.6 ± 8.7	26.2 ± 4.9	29.0 ± 4.5***	8.5 ± 6.3	d = 0.15 small
3000-m time trial (s)	829 ± 75	800 ± 69*	3.5 ± 4.5	806 ± 91	789 ± 81	1.0 ± 3.3	d = 0.63 medium

Values are means ± SD. * Presents significant within-group difference (* = $p < 0.05$, ** = $p < 0.01$, *** = $p < 0.001$).

TABLE 3. Mean (± SD) hormone concentrations for the hormonal contraceptive group (HC) and non-hormonal contraceptive group (NHC) before (PRE) and after (POST) the 10-week training period.

	HC			NHC			Effect Size
Variables	**PRE**	**POST**	**Δ%**	**PRE**	**POST**	**Δ%**	**Cohen's d**
TT (nmol/l)	0.72 ± 0.43	0.50 ± 0.19	88 ± 291	0.48 ± 0.32	0.54 ± 0.25	7 ± 70	d = 0.38 small
FSH (mIU/ml)	6.7 ± 4.8	6.0 ± 4.3	178 ± 310	8.6 ± 2.9	7.1 ± 2.6	-5 ± 21	d = 0.83 large
LH (mIU/l)	2.8 ± 1.9[a]	3.6 ± 2.5	616 ± 1697	7.6 ± 2.9[a]	5.4 ± 1.9*	-8 ±79	d = 0.52 medium
E (pmol/l)	116 ± 53	125 ± 39[aa]	89 ± 187	316 ± 378	341 ± 242[aa]	51 ± 91	d = 0.26 small
P (ng/ml)	0.34 ± 0.09	0.29 ± 0.11	2 ± 40	0.40 ± 0.27	0.38 ± 0.23	27 ± 64	d = 0. 47 small
SHBG (nmol/l)	137 ± 99	119 ± 87	-7 ± 13	68 ± 28	70 ± 22	8 ± 24	d = 0.78 medium
C (nmmol/l)	580 ± 160	607 ± 140	-6 ± 10	469 ± 119	491 ± 186	2 ± 27	d = 0.39 small
IGF-I (nmol/l)	32 ± 6	31 ± 8	10 ± 28	27 ± 8	27 ± 8	0 ± 19	d = 0.41 small

Values are means ± SD. * represents significant within-group difference (*p < 0.05, ***p < 0.01, ***p < 0.001). (HC: n = 9, NHC: n = 9) while [a] and [aa] represent significant between group differences p < 0.05 and p < 0.001, respectively. Total testosterone (TT), follicle stimulating hormone (FSH), luteinizing hormone (LH), estrogen (E), progesterone (P), sex-hormone binding globulin (SHBG), cortisol (C), and insulin-like growth-factor I (IGF-I).