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Research paper

Thyroid hormonal responses to intensive interval versus steady-state endurance exercise sessions

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ABSTRACT

OBJECTIVE: To compare the thyroid hormonal responses to high-intensity interval exercise (IE) and steady-state endurance exercise (SEE) in highly trained males (n=15). DESIGN: The IE session consisted of repeated periods of 90-seconds treadmill running at 100-110% VO_{2max} and 90-seconds active recovery at 40% VO_{2max} for 42-47 minutes. The SEE session was a 45-minute run at 60-65% VO_{2max}. Total work output was equal for each session. A 45-minute supine rest control session (CON) was also performed. Pre-session (PRE), immediate post-session (POST), and 12-hours post-session (12POST) blood samples were collected and used to determine free (f) T_4, fT_3, reverse (r) T_3, and cortisol levels. RESULTS: All PRE hormone levels were within clinical norms and did not differ significantly between sessions. All POST IE and SEE hormone levels were significantly elevated compared to POST CON ($p<0.001$). At 12POST, no significant differences between CON and SEE hormonal levels were observed; however, fT_3 was significantly reduced and rT3 was significantly elevated in 12POST IE compared to 12POST SEE and CON ($p=0.022$). For IE, at 12POST a negative correlation ($r_s = -0.70$, $p<0.004$) was found between fT_3 and rT_3. Also, for IE, a positive correlation ($r_s = 0.74$, $p<0.002$) between cortisol POST and rT_3 12POST was noted, and a negative correlation ($r_s = -0.72$, $p<0.003$) between cortisol POST and fT_3 12POST. CONCLUSION: IE results in a suppressed peripheral conversion of T_4 to T_3 implying that a longer recovery period is necessary for hormonal levels to return to normal following IE compared to SEE. These findings are useful in the implementation of training regimens relative to recovery needs and prevention of over-reaching - overtraining.

Key Words: Endocrine, Overtraining, Physical activity, Sports training, Stress

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INTRODUCTION

The major thyroid hormones (T_4, T_3) are critical to normal physiological function throughout life. This is especially true for T_3 since it is the principal biologi-

cally active form of the thyroid hormones. Physical exercise is known to affect the thyroid hormones. For example, prolonged-intense endurance exercise (e.g., >25 km competitive runs) or low-moderate intensity activity for extended periods (e.g., days of military field operations) results in a transient non-pathological hypothyroidism (i.e., a deficiency of thyroid hormone) lasting for 24 hours up to 72 hours.[1,2] Hypothyroidal conditions can compromise a person's health status and, relative to athletes, negatively impact the adaptation process associated with the myoplasticity of skeletal muscle, fundamental to the training progression and improvement in physical performance.[3] The cause of this exercise-induced hypothyroidism is unresolved; however, it has been hypothesized to be due to increased target tissue uptake, reduced peripheral conversion of T_4 to T_3, and/or reduced secretion from the thyroid gland due to circulating inhibitory factors released during exercise.[4,5]

Athletes habitually use numerous forms of exercise and training techniques in their regimes to improve performance. For example, for runners and swimmers it is common to use interval-style repetitions of relatively short duration at a near-maximal or supra-maximal level of intensity.[3,6] Currently, high-intensity interval training has gained attention because of its effectiveness in triggering adaptative mechanisms in the metabolism of skeletal muscle and an increase of VO_{2max}.[7] The influence of such forms of exercise on thyroid status has been studied only on a limited basis, with most studies reporting equivocal results (see review).[8] In part, this absence of clear findings is due to lack α of controls in research studies for extraneous factors that can affect thyroid hormones, such as dietary intake, prior physical activity, psychological stress, physical training status, and/or health status. Furthermore, in many studies that have examined thyroid responses to exercise, the total levels of the hormones are measured rather than the free level component. This is a critical oversight in study designs because, as mentioned above, the free hormone component is the biologically active form of the thyroid hormones. With all of this in mind, we sought to examine the influence of high-intensity interval exercise (IE) in comparison to sub-maximal, steady-state endurance exercise (SEE) on the free T_3 and free T_4 responses of highly trained male athletes. We hypothesized that IE exercise would place more physiological demands and stress on the athletes and result in a greater transient disturbance in the thyroid hormone levels, that is, hypothyroidism. Additionally, in order to access the stress aspects we concurrently measured cortisol responses in our subjects.

METHODOLOGY

Subjects. Fifteen male subjects were recruited for participation, all of whom had been engaged in consistent sports training for at least four years prior to the study. All subjects gave their written informed consent prior to participation in accordance with the Helsinki Declaration. Subject characteristics were as follows (mean ± SE): age = 27.2 ± 1.2 years, height = 177.6 ± 4.0 cm, mass = 72.6 ± 2.5 kg, percent body fat = 15.9 ± 2.0 % (skinfold assessment),[9] body mass index (BMI) = 23.0 ± 1.7 $kg \cdot m,^2$ and maximal oxygen uptake (VO_{2max}) = 4.36 ± 0.29 L $O_2 \cdot min.^1$

Screening - Graded Exercise Test. Each subject initially reported to our laboratory and underwent a preliminary physical examination to determine the normality of their pulmonary, circulatory, and orthopedic functioning. Subjects then performed a graded exercise test to determine their VO_{2max}. The graded exercise test required the subject to run on a treadmill with increases in grade and/or speed every three minutes until the subject reached volitional fatigue, or until there was an indication that VO_{2max} had been reached based upon previously published criteria.[10]

Experimental Sessions. Following the initial visit described above, the subjects reported to the laboratory at 17:30 hours on three separate days for a resting-control session (CON), SEE session, and an interval exercise session (IE). The order of administering the experimental sessions (CON *vs.* IE vs. SEE) was counterbalanced to prevent a systemic order effect, and all sessions were separated by 72 hours. In addition, subjects were required to abstain from exercise training, excessive emotional stress, and sexual activity for the 24 hours prior to each testing session, as well as report for each session having fasted for 4 hours. During each of these three laboratory sessions, the subjects first rested quietly in a supine position for half an hour. At approximately 18:00 hours, a 5 mL

pre-session (PRE) blood sample was taken. For the control session, this initial blood draw was followed by a 45-minute period of quiet supine rest, after which a 5 mL blood sample immediate-post session (POST) was taken. For the endurance session, the 45-minute rest period was replaced by 45 minutes of continuous treadmill running at 60-65% of VO_{2max}; blood samples were again drawn pre- and post-session. During the interval session, the subjects performed a series of intense 90-second anaerobic interval (~100-110% VO_{2max}) runs on a treadmill, alternating with 90-second recovery intervals of easy running (~40% VO_{2max}). The actual total exercise time for the interval session varied with each subject, but was between 42 and 47 minutes. As before, blood samples were drawn pre- and post-session. It is important to note that the number of intervals (exercise + recovery) in this session was calculated to equal the work output of the endurance session, thus the total work performed in both exercise sessions was identical. Finally, following each of the three experimental sessions, a single 5mL blood sample 12-hours post-session (12POST) was taken at approximately 07:00 hours on the morning of the next day.

Blood Analytical Methods. Blood specimens were collected using venipuncture procedures (antecubital vein) involving the use of a 10 cc syringe equipped with a 25g - 2.5 cm needle. All subjects were familiar with this procedure having served as research subjects in previous studies. Whole blood was immediately transferred to an EDTA treated Vacutainer® tube and placed on ice until later processing. Hematocrit and hemoglobin concentrations were obtained from whole blood samples so as to account for plasma volume shifts and the exercise effects of hemoconcentration. The methods of determination for these procedures have been described in detail elsewhere.[11] The Dill and Costill method was used with these hematocrit and hemoglobin measurements in the calculation of plasma volume shift to determine change in post-session measured to that of pre-session.[12] The remainder of each whole blood specimen was centrifuged at 3000 x *g*, 4˚C and stored at -50˚C until later biochemical analysis.

Hormonal measurements consisted of cortisol and the thyroid hormones: free (f) T_4 (fT_4), fT_3 (fT_4), and reverse T_3 (fT_4), (rT_3). These measures were determined by radioimmunoassay procedures (Diagnostic Systems Laboratories, Inc., Webster, TX; DPC Inc., Los Angeles, CA). All assay measurements were done in duplicate determinations, and between- and within-assay coefficients of variance were less than 10% in compliance with literature recommendations.[13]

Statistics. This study used a repeated measures design in which all subjects underwent all treatment conditions (sessions), and the treatments were administered in a counterbalanced randomized order. All hormonal responses (concentrations) were expressed as a percentage (%) of respective PRE values for the purposes of the statistical analyses. The percentages of changes were calculated using the following equations:

$$\text{POST (\%)} = ((\text{POST} - \text{PRE})/\text{PRE}) \times 100$$
$$\text{12POST (\%)} = ((\text{12POST} - \text{PRE})/\text{PRE}) \times 100$$

Statistically, a 3 (session type; CON, SEE, IE) x 2 (blood sampling time; POST, 12POST) completely repeated measures analyses of variance (ANOVA) was used to examine the hormonal responses. To insure the validity of the ANOVA analyses, Levene tests for homogeneity of variance and Greenhouse-Geisser adjustments for sphericity were utilized.[14,15] Fisher *LSD* post hoc tests were used to determine individual mean differences when significant F-ratios were found within the ANOVA analyses. Additionally, Spearman correlation coefficients (r_s) were calculated to examine the inter-relationship between the hormones. All statistical significance was set at $p \leq 0.05$.

RESULTS

The range for resting (pre-session) hormonal levels was as follows: fT_4 = 0.7 – 1.5 ng/dL, fT_3 = 230 – 620 pg/dL, rT_3 = 0.11 – 0.32 ng/mL, and cortisol = 178 – 368 nmol/L. In the resting (PRE) measurements there were no significant differences among sessions for any of the hormones. Furthermore, all hormonal values across all experimental sessions were normal and of a level expected for resting states.[16]

The hormonal responses to the experimental sessions are depicted in Figures 1-4. Significant ANOVA interaction effects ($p < 0.001$) for all hormonal analyses were detected and are discussed in the following section.

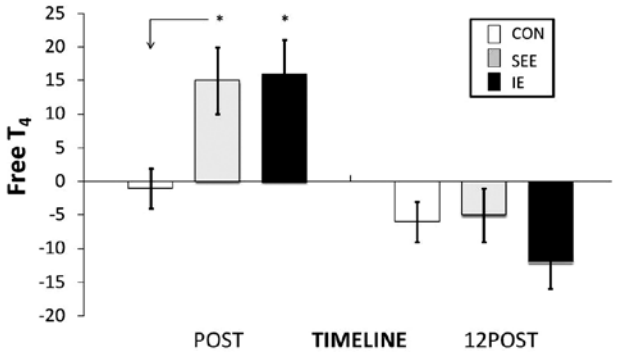

Figure 1. Free thyroxine (fT_4) relative change (%) responses to high-intensity interval exercise (IE), steady-state endurance exercise (SEE) and a rest control session (CON) in highly trained males (n=15). Values are means ± SE. The * denotes significant ($p<0.05$) changes for respective session mean values from the mean value denoted by the arrow within a specific measurement time (POST or 12 POST).

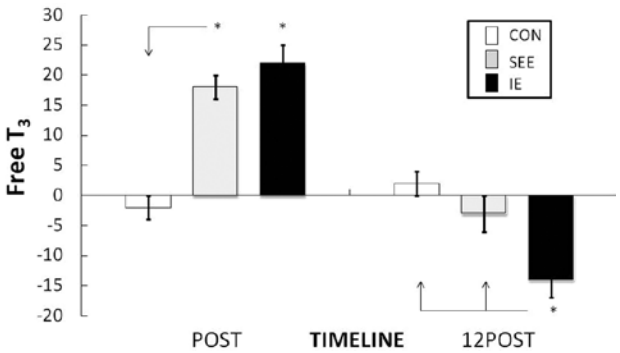

Figure 2. Free triiodothyronine (fT_3) relative change (%) responses to high-intensity interval exercise (IE), steady-state endurance exercise (SEE) and a rest control session (CON) in highly trained males (n=15). Values are means ± SE. The * denotes significant ($p<0.05$) changes for respective session mean values from the mean value denoted by the arrow within a specific measurement time (POST or 12 POST).

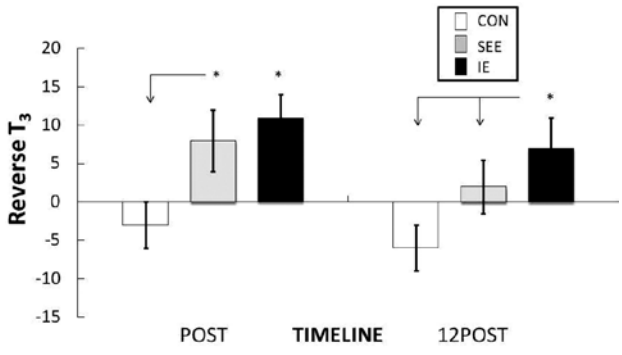

Figure 3. Reverse triiodothyronine (rT_3) relative change (%) responses to high-intensity interval exercise (IE), steady-state endurance exercise (SEE) and a rest control session (CON) in highly trained males (n=15). Values are means ± SE. The * denotes significant ($p<0.05$) changes for respective session mean values from the mean value denoted by the arrow within a specific measurement time (POST or 12 POST).

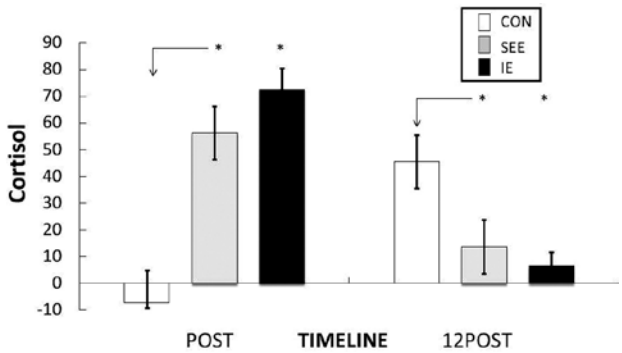

Figure 4. Cortisol relative change (%) responses to high-intensity interval exercise (IE), steady-state endurance exercise (SEE) and a rest control session (CON) in highly trained males (n=15). Values are means ± SE. The * denotes significant ($p<0.05$) changes for respective session mean values from the mean value denoted by the arrow within a specific measurement time (POST or 12 POST).

For fT_4 both IE and SEE resulted in a significant similar increase from the CON POST, but at 12POST no differences existed between the sessions (although IE responses tended to be more reduced [$p<0.069$]). The fT_3 displayed somewhat similar responses, as both IE and SEE resulted in significant similar increases from the response for CON POST. At 12POST, however, the IE fT_3 response was significantly reduced from that observed for CON and SEE. The rT_3 responses for both IE and SEE were significantly greater than the CON at POST. Conversely, at the 12POST measurement, rT3 was significantly greater than the response for both the CON and SEE session. At POST, the cortisol response was significantly increased for both the IE and SEE sessions (IE > SEE; $p<0.022$), and levels decreased significantly below CON levels at 12POST for both the IE and SEE sessions (not different from one another).

There were several pertinent correlations found. For the IE session 12POST measurements, a negative correlation ($r_s = -0.70$ $p<0.004$) was found between the reduction in fT_3 and elevation in rT3. Further-

more, for the IE session, a positive correlation (r_s = 0.74, $p<0.002$) was found between the elevation in cortisol at POST and the elevation of rT_3 at 12POST; and, a negative correlation (r_s = -0.72, $p<0.003$) for the elevation in cortisol at POST and the reduction in fT_3 12POST.

Significant plasma volume shifts occurred at POST for both IE and SEE (-9.9±1.0%, -11.2±2.2%) as compared to CON (-3.0±1.0%), but did not differ from one another. At 12POST there was a significant hemodilution effect with increases in plasma volume shifts for both IE and SEE (+4.9±1.4, +6.1±2.2%; not different from one another) versus CON (+0.5±0.9%). The hormonal values reported above were not, however, corrected for the plasma volume shifts as has been recommended in the literature.[17] Nonetheless, the hormonal responses to exercise were all essentially greater than the plasma volume changes observed, suggesting that endocrine responses were not merely the consequences of vascular fluid shifts.

DISCUSSION

The intention of this study was to examine the influence of high-intensity interval exercise as compared to sub-maximal, steady-state endurance exercise on the thyroid hormonal responses of highly trained athletes. Specifically, it was hypothesized that the high-intensity interval exercise would create a transient hypothyroidal state during the recovery period. Relative to fT_3, the more biologically critical of the thyroid hormones, this was the case as significantly reduced levels of the hormone were observed at 12 hours into recovery. To our knowledge, this is the first time this influence of high-intensity interval exercise on thyroid hormones has been demonstrated.

Others researchers have found decreases in thyroid hormones in response to physical exercise. Relative to sports scenarios, these studies have focused upon prolonged endurance activities such as treadmill running for a few hours or marathon running.[1,18] In many respects these activities have undue elements of fatigue associated with the exercise (i.e., running to exhaustion or a competitive event). For example, Moore and associates demonstrated that prolonged distance running to exhaustion would result in a hypothyroidal state up to 24 hours into recovery. The magnitude of the hormonal decline, which these and other researchers reported, is greater than that in the present study, but the trend in hormonal changes in each of the studies is quite similar. The differences in the magnitude of responses between the studies are most likely due to the differences in the duration of the exercise conducted and the overall greater energy demand on the subjects.[4]

As in the present study, Moore and associates also found a significant relationship between the decrease in fT_3 and exercise-induced elevations in cortisol.[1] They speculate that the reduction in fT_3 may be due to an inhibition of the peripheral conversion of T_4 to T_3 since cortisol is known to inhibit the 5'-deiodinase enzyme responsible for the conversion. In light of our significant correlation between fT_3 and cortisol in the IE session, we too speculate that such an event may be taking place in our subjects. This interpretation is further supported by the increase in rT_3 which we observed following IE. That is, the inhibition of the 5'-deiodinase enzyme results in greater amounts of T_4 undergoing peripheral conversion to rT_3 (a less biologically active thyroid form) rather than T_3 due to a reciprocal increase of the 5-deiodinase enzyme which catalyzes the T_4 to rT_3 conversion. Our data do suggest that such events have a temporal lag-time (cortisol POST vs. 12POST fT_3 and rT_3) which is feasible as physiologically one would not expect these pathways to be affected instantaneously. Such a temporal lag-time association has been proposed by others.[1,11] Also, relative to our cortisol data, we had speculated that the IE exercise session would create a greater stress in our subjects than the SEE based upon previous findings.[19] This view was supported by the trend towards significantly greater cortisol response POST in the IE than in the SEE session.

In non-sports activities, such as military training exercises, reports indicate that several days of low to moderate intensity physical activity can reduce thyroid hormones to a extreme hypothyroidal state i.e. to a much greater decline than that observed within the present study.[2,20,21] It should be noted however that these studies are complicated by the confounding influences of reduced caloric intake, high emotional stress, and a lack of adequate sleep, that is, all factors associated with substantial suppression of thyroid

function.[17,18] In the present study steps were taken to insure that the subjects consumed sufficient amounts of food so that they were not in a negative caloric state following all exercise sessions. Furthermore, all subjects reported that they maintained their normal sleep patterns (7.5-9.0 hours nightly) throughout the study and experienced minimal life stresses. Thus, the reduction in thyroids which we observed was not likely due to such factors as reported in the above mentioned studies on military training exercises.

Intensive interval training is an integral part of many sports training regimens, especially among high level competitive athletes. Additionally, it is very likely that during certain phases of training, high level athletes will participate in multiple training sessions within a 24-hour period, this resulting in less than 12 hours of recovery in between training sessions.[3,6] The present findings suggest that in such situations, if IE is utilized 12 hours is not enough time for the return to a normal, resting thyroid status. It is unclear, however, if subsequent exercise sessions of equal intensity would have an additive effect (i.e., a further reduction in thyroid hormones occurring – "downward staircase effect"). We plan to pursue evaluating the occurrence of such potential phenomena developing.

The current findings do unmistakably indicate that it is important for clinicians, if they are evaluating athletes via blood work, to know what exercise type they did in the previous workout session prior to coming to their office and when the session was conducted. If not, there is the potential of diagnosing a thyroid endocrine abnormality based upon the transient changes associated with exercise training (NB: the thyroid response to IE in the current study was transient since in the sessions that occurred after the IE session, 72 hours later, no significant disturbance in thyroids at rest was observed).

Furthermore, the current findings have important implications with regard to the detection of over-reaching – overtraining in athletes. Numerous studies have examined potential hormonal biomarkers that could reflect when appropriate levels of exercise training move to an inappropriate level of stress on the athlete (i.e., over-reaching or overtraining).[22-24] While not highly practical, as thyroid hormone assessments are not easily or inexpensively done, Lehmann and associates have proposed that the reduction in thyroid hormones in response to intensive training could be used as a biomarker indicative of when adequate levels of rest and recovery have not been provided.[22] The current findings are supportive of this notion. In addition, our findings are strengthened by the research design we employed incorporating a resting-control comparison session (i.e., previous research has not used this extra design step to substantial experimental effect. Therefore, for the athlete having biomarker evaluation performed, an exercise-induced hypothyroidal state would suggest that disruption in the endocrine system may exist; thus, adequate rest to allow for homeostasis of the endocrine system to be re-established has not occurred. We suggest that further research is necessary and warranted on this potential application of our current findings along these biomarker lines.

In conclusion, our findings indicate that intensive interval exercise results in a suppressed peripheral conversion of T_4 to T_3, as compared to a comparable amount of steady-state, sub-maximal endurance exercise. This occurrence implies that a longer recovery period is necessary for thyroid hormonal levels to return to normal following intensive interval exercise to allow for any transient hypothyroidal state that may develop to abate. Since low thyroid hormone levels are potential biomarkers for over-reaching – overtraining, the present findings could have implications for the implementation of training regimens relative to the rest and recovery needs of the athlete.

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