Serum concentrations of thyrotropin, thyroxine, triiodothyronine and thyroxine binding globulin in female endurance runners and joggers

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Abstract. The effects of endurance training and season on the function of the anterior pituitary-thyroid axis were studied in 18 female runners and their 12 controls, and in 13 joggers and their 11 controls in Northern Finland, with a large seasonal difference in environmental factors. The serum concentrations of thyrotropin (TSH), thyroxine (T4), free thyroxine (fT4), triiodothyronine (T3), thyroxine binding globulin (TBG) and oestradiol (E2) were measured during one menstrual cycle in the light training season (autumn) and in the hard training season (spring). The responses of TSH to intravenous TRH stimulation were also measured in the luteal phase of the cycle during the hard training season. Endurance running did not affect the basal or TRH-stimulated serum TSH concentrations, while those of T4 and fT4 in runners were lowered in both seasons and that of T3 in the light training season in relation to control subjects. The serum concentrations of TBG were also significantly lower in runners than their controls in the luteal phase in both seasons. The effect of jogging on thyroid hormones was less pronounced. Serum concentrations of TSH, T4, fT4, T3 and TBG were generally slightly higher in spring than in autumn. Strenuous endurance training seems to have minor changes on the function of the thyroid gland. Depressed T4 levels in runners may rather be due to lowered TBG levels than due to direct effect of training. In spring the function of anterior pituitary-thyroid axis is more active than in autumn.

The hypothalamic-pituitary-thyroid axis is sensitive to stress. During pregnancy the function of the thyroid gland increases (Burrow 1975), while in non-thyroidal illnesses, including infections, renal and hepatic diseases and starvation, the serum concentration of triiodothyronine (T3) decreases and that of serum thyroxine (T4) show minor alterations (Schimmel et al. 1977).

Endurance training is a hard physical stress which decreases the amount of body fat and increases demands on the energy supply, and which is partly regulated by thyroid hormones. Secretion of thyrotropin (TSH) is also under the stimulatory control of oestrogens (Labrie et al. 1978), the concentrations of which, however, are decreased in female runners (Boyden et al. 1983; Ronkainen et al. 1985). Physical exercise may thus affect the function of the anterior pituitary-thyroid axis of women by different mechanisms. The effects of such training on the pituitary-thyroid axis have been evaluated only in few investigations, dealing with ballet dancers (Warren 1980) and runners (Boyden et al. 1982, 1984; Marcus et al. 1985). The results in these studies have been conflicting; decreased, unchanged or increased responses of TSH and thyroid hormones to strenuous exercise have been reported.

To gain information on the association of the function of the pituitary-thyroid axis and chronic, intense training in women, we measured serum concentrations of TSH, thyroid hormones, thyroxine binding globulin (TBG) and oestradiol (E2) of runners, joggers and their control subjects in autumn and spring, characterised by different training activity of the runners.
Subjects and Methods

Eighteen competitive endurance runners of national standard, at a mean (± SD) age of 20 ± 4.4 years and 12 non-competitive control women (21.0 ± 2.4 years) participated in this study in the light training season in autumn and in the hard training season in the following spring. In addition, 13 recreational joggers (31.2 ± 4.1 years) and their 11 control women (29.1 ± 3.4 years) were studied. The study persons were eumenorrheic and used no hormonal medication. The results concerning the functions of the pituitary-ovarian axis (Ronkainen 1985; Ronkainen et al. 1985) and the adrenal cortex (Ronkainen et al. 1986) of the women participating in this trial have been reported elsewhere.

The middle- and long-distance runners belonged to the 10 best in their age group in Finland; 7 were members of the Finnish National Track and Field Team. The joggers had run regularly for 3–10 years and jogged 2 to 5 times 15–60 km weekly. The control women did not participate in any regular physical activity.

The skinfold thicknesses (biceps, triceps, subscapularis) of the subjects were measured with a Harpenden skinfold caliper, and the percentage of body fat was determined using Siri's formula. At the beginning of the study in the autumn the runners had significantly less (P < 0.001) body fat than their controls, 22.1 ± 3.3% and 27.7 ± 3.5%, respectively, and the percentage of body fat in runners decreased to 19% (P < 0.01) with training. There were no differences in other groups (range 25.1–28.1%).

Blood samples for the determinations of serum TSH, T₄, fT₄, T₃, TBG and E₂ were drawn at 08.00–09.00 h on days 7–8, 12–13, 14–15, 20–21 and 22–23 of the menstrual cycle in the light (September–October) and hard training (April–May) seasons. The subjects were instructed not to run on the evening before blood sampling. After centrifugation, the serum samples were stored at −20°C before assay.

TRH-stimulated serum TSH levels were examined in the late luteal phase (days 24–25) of the menstrual cycle in the hard training season.

Blood samples were obtained through an in-dwelling forearm catheter before and 20, 60, 80 and 120 min after the iv injection of 200 µg of TRH (Hoffman-La Roche, Basle, Switzerland).

Assays

Serum TSH, T₄, T₃ and E₂ concentrations were measured by radioimmunoassays using reagent kits obtained from Farmos Diagnostica (Turku, Finland). The sensitivity of the TSH assay was 0.5 mU/l, the coefficient inter-assay variation was 5.4%, and the coefficient of intra-assay variation was 3.4%. The respective values were 5 nmol/l, 5.7%, and 4.5% for the T₄ assay, 0.1...
and seasons. Controls differed significantly from the joggers and their controls, as well as from the controls, between autumn and spring. The concentrations were with the same 7-8 and 12-15 mg/l for T3 assay and 0.03 nmol/l, 9.7% and 8.0% for the T4 assay. Serum fT4 was measured using radioimmunoassay kits obtained from Diagnostic Products Corporation, Los Angeles, CA. The sensitivity was 0.13 pmol/l, the inter-assay variability was 5.6%, and the intra-assay variability was 4.4%.

Serum TBG was measured using reagent kits from Behringwerke AG, Malburg, FRG. The sensitivity of the assay was below 2 mg/l, the inter-assay variability was 3.6% and the intra-assay variability 2.1%.

All samples of each test subject were analysed in the same RIA. The reference values for adult women in our laboratory are below 5.3 mU/l for serum TSH, 55-130 nmol/l for T4, 10.8-21.5 pmol/l for fT4, 1.0-2.6 nmol/l for T3 and 16-28 mg/l for TBG.

Statistics
Student's two-tailed t-test was used to compare the results from the runners and their controls, and from the joggers and their controls separately. The two-tailed paired t-test was used to test differences between autumn and spring values in each of the groups separately. Because the distribution of TSH results was not symmetrical, non-parametric Mann-Whitney and Kruskal-Wallis tests were used to compare the runners and their controls in autumn and spring, and the joggers and their controls, respectively. The comparison of autumn and spring values within each group was made with the non-parametric Wilcoxon test.

Results

The effect of physical exercise on serum TSH and thyroid hormone levels

The mean concentrations of serum TSH did not differ between the runners and their controls (Fig. 1), or between the joggers and their controls (Fig. 2) at any time of the menstrual cycle in both seasons.

The responses of serum TSH to TRH did not differ significantly between the runners and their controls or between the joggers and their controls (Fig. 3).

Compared with their controls the runners had significantly lower serum concentrations of thyroid hormones; T4 in the follicular and luteal phases of the menstrual cycle in both seasons, fT4 during the follicular phase in spring and during the luteal phase in autumn, and T3 during the luteal phase in autumn (Fig. 1).

The joggers had significantly lower concentrations of fT4 on days 22-23 in autumn and on days 7-8 in spring than their control subjects (Fig. 2).

The serum concentrations (mean ± SEM) of TSH, T4, fT4, T3 and TBG in joggers and their controls in autumn and spring. The horizontal lines with asterisks indicate significant differences between the serum concentrations in each group in autumn and spring.

\[ *P < 0.05, **P < 0.01 \]
Mean (± SEM) concentrations of TSH at the end of the hard training period during the late luteal phase of the menstrual cycle in the TRH test. TRH (200 µg) was injected at time zero.

The mean concentrations of TBG were significantly lower in the runners than in their controls in the luteal phase of the menstrual cycle both in the light and hard training seasons (Fig. 1).

There were no differences in TBG levels between the joggers and their controls (Fig. 2).

The effect of physical exercise on serum E₂ levels
The mean concentrations of E₂ were significantly lower in the runners (0.14 ± 0.02 (± s.e.) nmol/l) than their controls (0.23 ± 0.03 nmol/l, P < 0.05) on days 22–23 in light training season. In hard training season the runners had lower E₂ concentrations than their controls on days 12–13 (0.15 ± 0.03 vs 0.42 ± 0.11 nmol/l, P < 0.05) and on days 22–23 (0.29 ± 0.05 vs 0.54 ± 0.07 nmol/l, P < 0.01). The mean concentrations of E₂ did not differ between the joggers and their controls.

The effects of season on serum TSH and thyroid hormone levels
The serum concentrations of TSH were significantly higher in spring in runners and their controls in the follicular and luteal phases, in joggers at mid-cycle and in their control subjects in the follicular phase of the cycle, in relation to the respective autumn results (Figs. 1 and 2).

The runners had significantly higher serum concentrations of T₄ and T₃ during the luteal phase, and the control subjects of the runners had significantly higher serum T₄ at mid-cycle, in spring than in autumn (Fig. 1).

The joggers had significantly higher serum concentrations of fT₄ during the luteal phase in spring than in autumn (Fig. 2).

The concentrations of TBG in the runners were higher on days 7–8, 12–13 and 20–21 in spring than in autumn (Fig. 1), and those of the controls of the joggers on days 14–15 (Fig. 2).

Discussion
In our study the endurance runners and joggers had unchanged serum concentrations of TSH, as Boyden et al. (1982) also described in joggers, and Warren (1980) in ballet dancers. In runners, with exhaustive training activity, TSH secretion has been reported to be increased (Boyden et al. 1984). The reason for the difference between our results and those of Boyden et al. (1984) might be the different intensity of training, because our runners, after an exercise programme of about 6 months, ran about 42 km weekly, whereas the runners in Boyden’s study were examined after 8.5–13.5 months’ training with actual running of 80 km weekly.

In our study, the TRH-stimulated TSH concentrations also remained similar in runners and their controls, and in joggers and their controls. Moderate endurance exercise thus seems not to alter the functional capacity of the pituitary thyrotropic cells. Different TSH responses to TRH in the two studies of Boyden et al. (1982, 1984) are probably also due to a different intensity of physical activity.

In contrast to TSH, the concentrations of thy-
roid hormones, especially that of $T_4$, were low in runners compared with non-running women, which agrees with a previous report (Marcus et al. 1985). Unchanged plasma $T_4$ levels, an unchanged $fT_4$ index, decreased $T_3$ (Boyden et al. 1982) and even increased $T_4$ levels (Boyden et al. 1984) have been found in other studies. In addition, serum $fT_4$ and $T_3$ have been significantly lower in amenorrhoeic, hypo-oestrogenic runners than in their sedentary controls (Marcus et al. 1985). Different intensities of exercise may also explain these controversial results. This concept is also emphasized by the present and previous (Boyden et al. 1982) findings showing that the changes in thyroid hormone concentrations of joggers were much less than those of the runners.

Synthesis of TBG in the liver is under the control of oestrogens (Dowling et al. 1960), and consequently its serum level decreases in hypo-oestrogenaemia. In our study, the endurance runners had suppressed ovarian activity with lowered serum concentrations of oestadiol (Ronkainen et al. 1985), which thus can explain why the TBG level in the runners was lower than that of the control women, a finding not to our knowledge reported previously. The oestrogen-dependent mechanisms thus seem to be at least partly responsible for the decreased concentrations of total thyroid hormones in running women.

Because the concentration of the active form of thyroxine, $fT_4$, changed with exercise less than that of $T_4$, bound mostly to TBG and other thyroxine-binding proteins, the risk of thyroidal hypofunction of female runners is minimal. The concentrations of $fT_4$ in runners and control subjects were largely similar. Hence the negative feedback signals of $fT_4$ to the thyrotrophs of the women in these two groups must have been similar, and consequently the serum concentrations of TSH did not differ between runners and their controls.

Serum TSH concentrations were generally higher in spring than in autumn. This finding agrees with some previous reports (Halberg et al. 1983; Konno et al. 1982), but not with all of them (Pasquali et al. 1984; Rastogi et al. 1976). A significant inverse relationship between basal TSH levels and the ambient temperature has been found (Konno et al. 1982), and it may partly explain the increased secretion of TSH in spring in our study, because the average temperature in October is higher than in March.

Small increases of serum thyroid hormone levels in the spring-time compared to autumn, found in this study, may be due to increased TSH secretion during this season. In another study, the highest circannual values of thyroid hormones were found in August-October in France (Pasquali et al. 1984), but there was no variation in Holland (Postmes et al. 1974) or in Japan (Konno et al. 1982).

In our study the serum concentration of TBG in spring was higher than in autumn in the runners and in the controls of the joggers. In other studies a seasonal variation of TBG has been absent (Rastogi et al. 1976), or its level has been high in autumn and low in March–July (Pasquali et al. 1984). The reason for the increased TBG level in spring in our study is unclear. It is possibly associated with the increased serum concentrations of oestrogens in spring (Ronkainen et al. 1985) and also with hard exercise, which when for many weeks carried out increased the concentrations of TBG (Opstad et al. 1984).

In conclusion, physical training may affect slightly the function of the thyroid gland without changing pituitary TSH secretion. In spring the function of the anterior pituitary-thyroid axis was activated.

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**References**


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