Effect of Dehydroepiandrosterone Sulfate on the Concentrations of Thyroxine and Triiodothyronine in Rats after Single or Repeated Cold Exposure

S. K. Saryg, T. A. Grigoreva, T. A. Obut, and T. U. Dementeva

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Repeated cold exposure (4°C) was followed an increase in the concentrations of total thyroxine, free thyroxine, and total triiodothyronine in blood plasma of male rats, while single cold exposure was accompanied by a significant increase only in the concentrations of total triiodothyronine and free thyroxine. After administration of dehydroepiandrosterone sulfate (30 mg/kg), the increase in total thyroxine and total triiodothyronine concentrations became more pronounced after repeated cold exposure, but not after single cold exposure. Dehydroepiandrosterone sulfate did not affect the concentration of free thyroxine after single and repeated cold exposure.

Key Words: *dehydroepiandrosterone sulfate; thyroxine; triiodothyronine; cold*

Dehydroepiandrosterone (DHEA) or DHEA sulfate (DHEA-S) is an androgenic hormone secreted by the zona reticularis of the adrenal cortex [3]. Our previous studies showed that DHEA-S produces a stress-limiting effect [1] and plays an adaptive role in the organism under conditions of repeated stress. However, little is known about the influence of DHEA-S on the thyroid system. This system may be involved in the adaptation of an organism. Published data show that DHEA affects the concentration of thyroid hormones [5]. For instance, injection of DHEA (50 mg/kg) into the hypothalamus of intact rat pups has a stimulatory effect on the level of thyrotropin-releasing hormone, which is accompanied by an increase in the concentrations of thyrotropic hormone and thyroxine. However, the effects of DHEA or DHEA-S on thyroid hormone concentration in adult rats during cold exposure remain unknown. Published data show that the concentration of DHEA-S is high patients with hyperthyroidism and low in hypothyroid subjects. These differences are probably related to the effect of thyroid hormones on activity of $P_{450\text{-}scc}$ enzymes, including 17-α-hydroxylase, $C_{17,20}$-lyase, and sulfate transferase. Little is known about the influence of DHEA-S on thyroid hormone activity.

Here we studied the effect of DHEA-S on the concentrations of total thyroxine (tT_4), free thyroxine (frT_4), and total triiodothyronine (tT_3) in male rats under conditions of single or repeated cold exposure.

MATERIALS AND METHODS

Experiments were performed on male Wistar rats weighing 200-260 g. Experimental groups consisted of 10-43 animals. The rats were maintained in a vivarium under standard conditions (Institute of Physiology, Siberian Division of the Russian Academy of Medical Sciences) and had free access to food and water. Intact animals served as the control. Cold exposure was performed one time or repeatedly for 19 days (1 h daily, 4°C). The blood was collected into heparinized tubes after decapita-

Institute of Physiology, Siberian Division of the Russian Academy of Medical Sciences, Novosibirsk, Russia. ***Address for correspondence:*** t.a.obut@physiol.ru. T. A. Obut

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tion of animals. The plasma was isolated by centrifugation. The concentration of hormones was measured immediately after treatment. The concentrations of tT_4, tT_3, and frT_4 in blood plasma were measured by radioimmunoassay with standard kits. DHEA-S in a dose of 30 mg/kg was administered 2 days before decapitation. The results were analyzed by Student's *t* test. The data are expressed as $M \pm m$.

RESULTS

The increase in tT_4 ($p<0.02$) concentration after repeated cold exposure was more pronounced in rats receiving DHEA-S ($p=0.002$). Similar results were obtained for tT_3. The concentration of tT_3 increased after cold exposure ($p=0.03$) and, particularly, under conditions of pretreatment with DHEA-S ($p=0.03$, Fig. 1). Hence, DHEA-S produced an additional thyroid-stimulating effect. Taking into account the fact that the level of DHEA-S is high during hyperthyroidism [4], reciprocally, an additional increase in the level of endogenous DHEA-S can be anticipated after repeated cold exposure accompanied by an increase in the concentrations of tT_4 and tT_3. However, this assumption requires further investigations.

DHEA-S was administered to animals of the control group to evaluate the effect of this substance on tT_4 and tT_3. No statistically significant changes were observed under these conditions. Hence, the tT_4/tT_3 ratio in rats after repeated cold exposure was similar to that in control animals receiving DHEA-S (significant increase, $p=0.001$).

As differentiated from repeated cold exposure, the concentration of tT_4 did not change after single cold stress alone or in combination with DHEA-S administration. However, the concentration of tT_3 significantly increased after single cold exposure alone ($p=0.02$) or in combination with DHEA-S pretreatment ($p<0.02$, Fig. 2).

The concentration of frT_4 significantly increased after repeated and single cold exposure ($p=0.003$ and $p=0.006$, respectively, compared to the control), which is consistent with published data that the concentration of frT_4 increases on days 1 and 5 of cold exposure (3°C) [2]. Pretreatment with DHEA-S had little effect on frT_4 concentration during single and repeated cold exposure (Fig. 3, *a*, *b*).

We conclude that DHEA-S potentiates the increase in the concentrations of tT_4 and tT_3 in male rats caused by repeated cold exposure, which confirms the thyroid-stimulating effect of DHEA-S under these conditions.

Single cold exposure was accompanied by a significant increase in the concentration of tT_3, but had no effect on tT_4. DHEA-S had little effect on the concentrations of tT_3 and tT_4 in animals during single cold exposure.

The concentrations of tT_4 and tT_3 in control animals remained practically unchanged after administration of DHEA-S. Therefore, DHEA-S is ineffective under control conditions.

The concentration of frT_4 significantly increased after repeated and single cold exposure. DHEA-S had no effect on frT_4 concentration under these conditions.

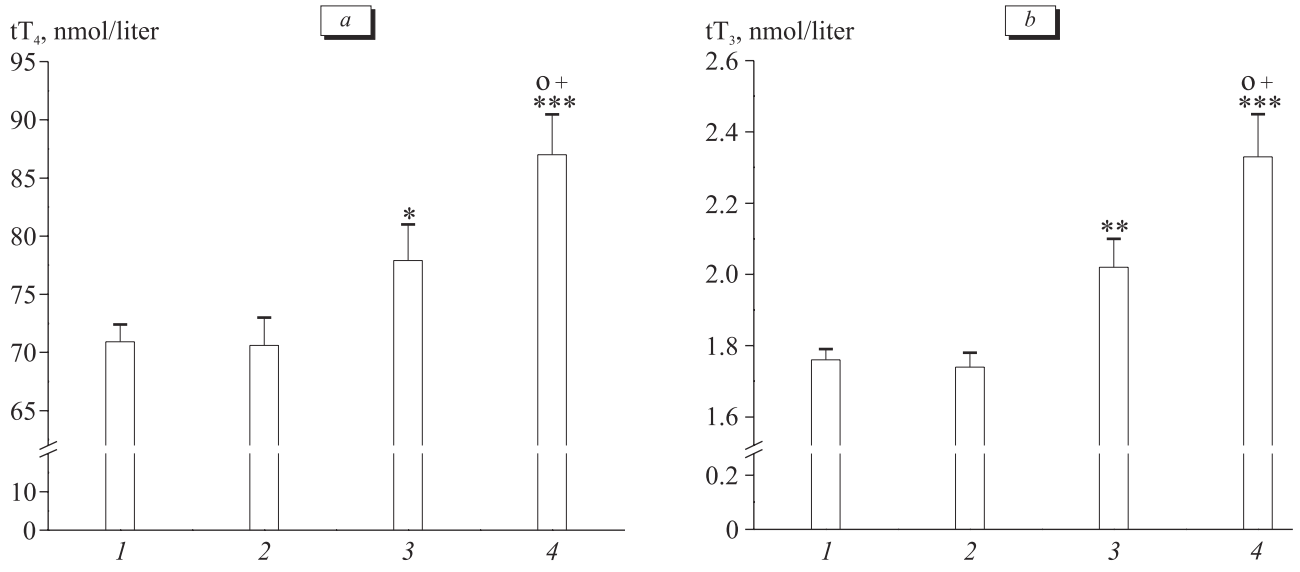

Fig. 1. Effect of repeated cold exposure and administration of DHEA-S on the concentrations of tT_4 and tT_3 in animals. Control (*1*); control+DHEA-S (*2*); 19-day cold exposure (*3*); 19-day cold exposure+DHEA-S (*4*). *$p<0.02$, **$p=0.002$, and ***$p=0.001$ compared to *1*; °$p=0.001$ compared to *2*; +$p=0.03$ compared to *3*.

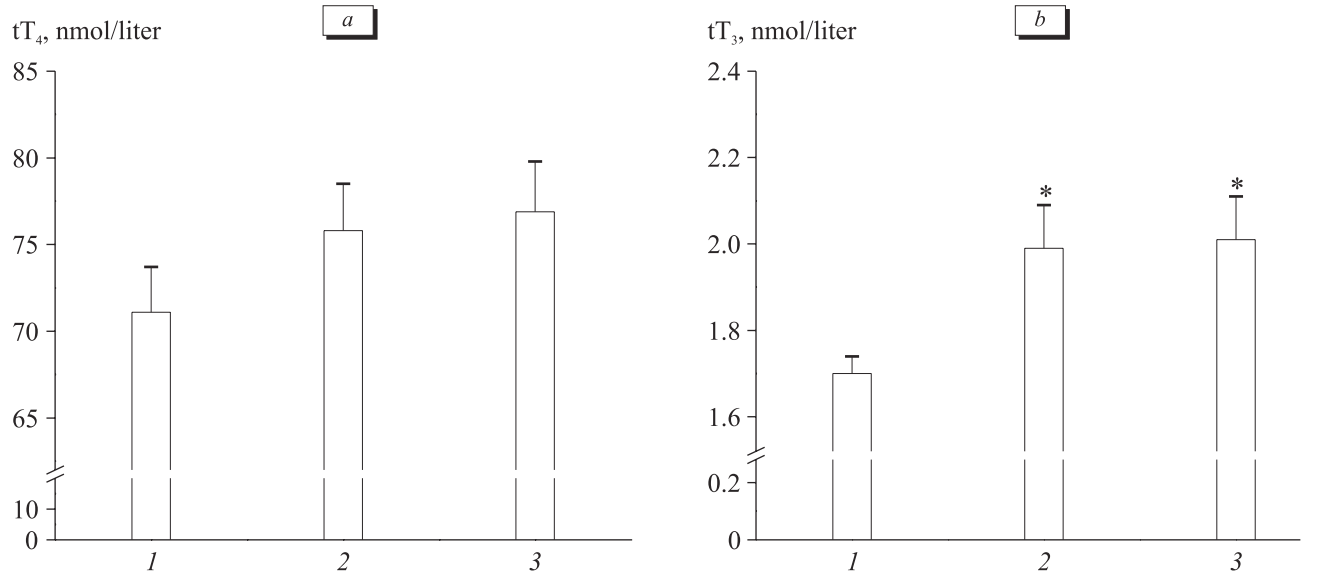

Fig. 2. Effect of single cold exposure and administration of DHEA-S on the concentrations of tT_4 and tT_3 in animals. Control (*1*); single cold exposure (*2*); single cold exposure+DHEA-S (*3*). **p*<0.02 compared to *1*.

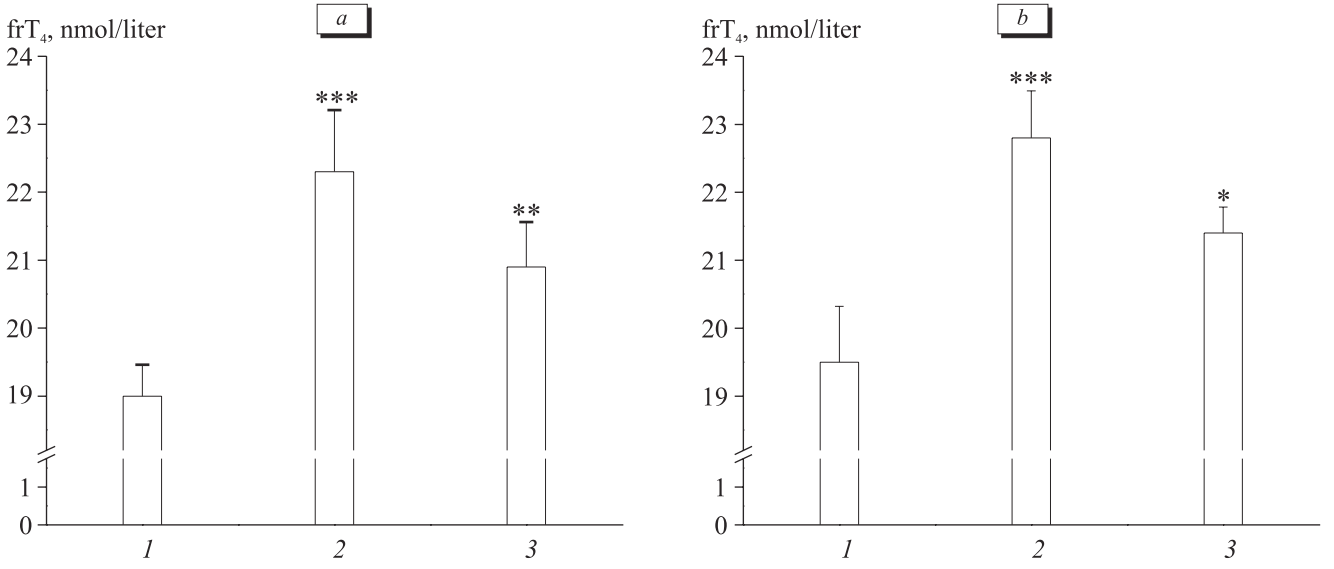

Fig. 3. Effect of repeated (*a*) or single cold exposure (*b*) and administration of DHEA-S on the concentration of frT_4 in animals. (*a*) Control (*1*); repeated cold exposure (*2*); repeated cold exposure+DHEA-S (*3*). (*b*) Control (*1*); single cold exposure (*2*); single cold exposure+DHEA-S (*3*). **p*<0.04, ***p*=0.02, and ****p*<0.01 compared to *1*.

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