PHYSIOLOGY

Thyroid Hormone Deficiency Determines Predisposition to Catalepsy in Rats

N. N. Barykina, V. F. Chugui, T. A. Alekhina, V. G. Kolpakov, E. A. Ivanova, A. V. Maksyutova, and A. V. Kulikov

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny,* Vol. 132, No. 7, pp. 13-15, July, 2001
Original article submitted March 12, 2001

The role of thyroid hormones in predisposition to cataleptic reaction was investigated. GC rats with genetic predisposition to catalepsy were characterized by decreased serum thyroxin content in comparison with Wistar rats. Thyroidectomy even more reduced the blood concentration of thyroxin in GC rats 30 days postoperation and augmented predisposition to catalepsy in both rat strains.

Key Words: *catalepsy; thyroxin; hypothyroidism*

The development of mental disorders in patients with thyroid dysfunction has been repeatedly described [5, 10], but the neurobiological mechanism of this phenomenon remains unclear. Behavioral changes in animals with thyroid dysfunction were revealed. Rats with thyroid hormone deficiency demonstrated longer immobility time in the forced swimming test [7]. Catalepsy or excessive immobilization reaction regarded as an adaptive passive defense strategy [2] in laboratory rats was markedly potentiated during long-term selection, which resulted in derivation of GC rat strain predisposed to this reaction [1].

The aim of the present study was to elucidate the relationship between the concentrations thyroid hormone and predisposition to catalepsy. To this end, we compared the concentrations of thyroid hormones in animals with genetically determined differences in the severity of catalepsy and evaluated the effect of thyroidectomy on manifestation of catalepsy in Wistar and GC rats.

Laboratory of Evolutional Genetics, Laboratory of Phenogenetics, Institute of Cytology and Genetics, Siberian Division of Russian Academy of Sciences, Novosibirsk. ***Address for correspondence:*** kulikov@bionet.nsc.ru. Kulikov A. V.

MATERIALS AND METHODS

Experiments were carried out on adult male Wistar (n=24) and GC (n=22) rats aged 2 months (200±10 g at the start of the experiment). In 12 Wistar and 10 GC rats the thyroid glands were removed under Nembutal (35 mg/kg) narcosis. Thyroidectomized rats were offered deionized water with 0.5% $CaCl_2$ throughout the experiment. Sham-operated Wistar (n=12) and GC rats (n=12) served as the control. All rats (4 per cage) were kept at 22°C and 12-h day/night cycle. Tests were carried out on day 31 postoperation. Catalepsy was evaluated by the time during which the animal retained a preset vertical posture at the corner of the cage and by the percentage of animals retaining this vertical posture for at least 10 sec [1]. The rats were decapitated 2 days after the test. Serum concentrations of total thyroxin (nM) were assayed with a TiroididIFA-Tiroksin kit for enzyme immunoassay (St. Petersburg). The data were expressed as $M\pm m$ and compared using ANOVA test with multiple comparison after Bonferroni.

RESULTS

The concentration of thyroxin in sham-operated GC rats was significantly lower than in Wistar rats (p<0.001,

0007-4888/01/1321-0620$25.00

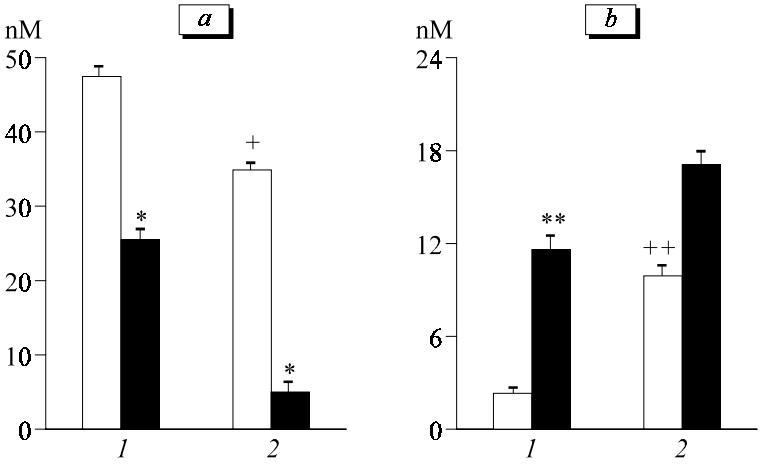

Fig. 1. Effect of genotype and thyroidectomy on serum concentration of total thyroxin (*a*) and time of cataleptic immobility (*b*) in rats. *1*) Wistar rats; *2*) GC rats; light bars: control; dark bars: thyroidectomy. **p*<0.001, ***p*<0.05 *vs.* sham-operated control; ^{+}p<0.001, ^{++}p<0.05 *vs.* Wistar rats.

Fig. 1, *a*). One month after thyroidectomy the concentration of thyroxin in GC rats decreased 7-fold (p<0.001, Fig. 1, *a*). In 5 of 7 thyroidectomized GC rats serum thyroxin concentration was below the sensitivity limit. In Wistar rats thyroidectomy 2-fold decreased serum thyroxin concentration (p<0.001, Fig. 1, *a*). It can be assumed that homeostasis of thyroid hormones in GC rats is unstable, and surgical removal of the gland is sufficient for almost complete elimination of thyroid hormones from the body within 1 month. We hypothesized that GC rats are characterized by hereditary hypothyroidism, but further studies including measurements of triiodothyronine and thyroid-stimulating hormone are needed for final conclusion. In Wistar rats metabolism of thyroid hormones is more stable, and thyroid hormones are not completely removed from the body one month after thyroidectomy. A more pronounced suppression of hormone production can be achieved by a combination of thyroidectomy and high doses of ^{131}I [3,4].

Thyroidectomy induced catalepsy in 7 of 12 Wistar rats (p<0.05). The time of immobility in thyroidectomized Wistar rats was longer than in sham-operated animals (p<0.05, Fig. 1, *b*). There was a trend to prolongation of immobility time in thyroidectomized GC rats compared to sham-operated GC rats (p<0.05, Fig. 1, *b*). Two-factor ANOVA revealed an appreciable contribution of the genotype ($F_{1.42}$=5.16, p<0.028) and thyroidectomy ($F_{1.42}$=8.09, p<0.0068) to determination of catalepsy time. On the other hand, no mutual effect of genotype and thyroidectomy on the immobility time was observed (p<0.05). These results are in line with published reports on increased immobility time in the forced swimming test in GC rats compared to Wistar rats [8] and in hypothyroid Wistar rats compared to the control [7]. It can be hypothesized that thyroid hormone deficiency is an important factor predisposing to catalepsy. However this hypothesis requires further experimental verification, in particular evaluation of the effects of chronic treatment with therapeutic doses of thyroid hormones on the severity of catalepsy in rats.

It was found that hereditary predisposition to catalepsy in rats and mice is associated with a lower density of type 2A serotonin receptors in the brain [9]. On the other hand, thyroidectomy markedly decreases the density of these receptors in rat brain [6]. Thus, thyroid hormone deficiency increases predisposition to catalepsy by reducing the density of type 2A serotonin receptors. Generally, catalepsy in hypothyroid animals is a convenient model for studying the relationship between thyroid dysfunction, neural processes, and behavioral abnormalities.

The study was supported by the Russian Foundation for Basic Research (grant No. 99-04-49945).

REFERENCES

1. N. N. Barykina, I. L. Chepkasov, T. A. Alekhina, and V. G. Kolpakov, *Genetika*, **19**, 2014-2021 (1983).
2. A. K. Dixon, *Br. J. Med. Psychol.*, **71**, 417-445 (1998).
3. M. B. Dratman, *The Thyroid Axis and Psychiatric Illness*, Eds. R. T. Joffe, A. J. Levitt, Washington (1993), pp. 3-94.
4. H. F. Escobar-Morreale, F. Escobar del Rey, M. J. Obregon, and G. Morreale de Escobar, *Endocrinology*, **137**, 2490-2502 (1996).
5. R. T. Joffe and A. J. Levitt, *The Thyroid Axis and Psychiatric Illness*, Eds. R. T. Joffe, A. J. Levitt, Washington (1993), pp. 195-253.
6. A. Kulikov, X. Moreau, and R. Jeanningros, *Neuroendocrinology*, **69**, 453-459 (1999).
7. A. Kulikov, J. Torresani, and R. Jeanningros, *Neurosci. Lett.*, **234**, 111-114 (1997).
8. E. M. Nikulina, N. K. Popova, V. G. Kolpakov, and T. A. Alekhina, *Biogenic Amines*, **4**, 399-406 (1987).
9. N. K. Popova and A. V. Kulikov, *Am. J. Med. Genetics*, **60**, 214-220 (1995).
10. A. J. Prange, *Thyroid*, **6**, 537-543 (1996).