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BRIEF COMMUNICATION

The Effect of Acute Nicotine Administration on Plasma Levels of the Thyroid Hormones and Corticosterone in the Rat

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CAM, G. R. AND J. R. BASSETT. *The effect of acute nicotine administration on plasma levels of the thyroid hormones and corticosterone in the rat.* PHARMACOL BIOCHEM BEHAV 19(3) 559–561, 1983.—The effects of a single intraperitoneal injection of nicotine hydrogen tartrate (200 μg/kg) on the plasma levels of thyroxine, triiodothyronine and corticosterone were monitored over a 24 hour period. Nicotine did not alter the plasma levels of either of the thyroid hormones but did produce a significant increase in plasma corticosterone, an effect which peaked at 20 min post-injection and lasted for 45 min.

Nicotine Thyroxine Triiodothyronine Corticosterone

NICOTINE, a major constituent of cigarette smoke, has been shown to influence many hormone systems associated with the regulation of activity and metabolism. Nicotine has been shown to stimulate a dramatic release of both catecholamines, noradrenaline and adrenaline, from the adrenal medulla [3,8]. Tjalve and Popov [16] noted that high concentrations of nicotine inhibited the glucose-induced insulin secretion from rabbit pancreatic islets, whereas lower concentrations of nicotine stimulated the secretion of the hormone. Such changes in insulin levels may account for the rise in blood glucose concentration reported following nicotine administration [10]. More recently nicotine has been shown to stimulate the release of ACTH from the pituitary gland, resulting in an elevated plasma glucocorticoid level [2].

There have been, however, very few reports on the influence of nicotine on the thyroid axis, even though the thyroid hormones play a major role in regulating activity and energy utilization. Histological studies of the thyroid gland from chronically nicotine treated animals have produced conflicting results varying from a suggested elevated thyroid activity [15], through no change in thyroid function [17] to degeneration and hypofunction [4]. There have been no direct studies on the acute effects of nicotine on the thyroid hormones.

The present study undertook to investigate nicotine's action on the plasma levels of the thyroid hormones, thyroxine (T_4) and triiodothyronine (T_3). Since there appears to be a close connection between thyrotropic and adrenocorticotropic activity [12], plasma levels of corticosterone were also measured.

METHOD

Animals

Adult male rats aged 100–110 days were housed in groups of three under conditions of constant temperature and humidity (21°C, 46% humidity) and subjected to a 12 hr reversed night day schedule (light 20.00–08.00), beginning at least 14 days prior to commencement of experimentation. Food and water were provided ad lib.

Triidothyronine and Thyroxine Assay

Triiodothyronine (T_3) and thyroxine (T_4) were assayed by radioimmunoassay kit supplied by the Radiochemical Centre, Amersham, England. The radioimmunoassay method depends on the competition for binding sites on a T_3 and T_4 specific antibody between the thyroid hormone in serum and ^{125}I-labelled hormone. The anti-T_3 serum had a

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TABLE 1

PLASMA TRIIODOTHYRONINE (T_3) CONCENTRATIONS OVER TIME FOLLOWING EITHER ON INTRAPERITONEAL INJECTIONS OF 200 μg/kg NICOTINE HYDROGEN TARTRATE OR SALINE

Time (min)	Plasma T_3 (μg l^{-1}) (mean ± s.e.) Nicotine	Saline	Unpaired *t*-test, $p >$
0	0.57 ± 0.01	0.59 ± 0.03	0.05
5	0.64 ± 0.02	0.59 ± 0.03	0.05
10	0.73 ± 0.02	0.70 ± 0.03	0.05
15	0.63 ± 0.02	0.59 ± 0.02	0.05
20	0.60 ± 0.02	0.60 ± 0.02	0.05
30	0.68 ± 0.01	0.66 ± 0.02	0.05
45	0.55 ± 0.01	0.59 ± 0.03	0.05
60	0.58 ± 0.03	0.61 ± 0.02	0.05
120	0.80 ± 0.02	0.81 ± 0.02	0.05
6 hr	0.80 ± 0.02	0.85 ± 0.02	0.05
24 hr	0.79 ± 0.04	0.85 ± 0.03	0.05

TABLE 2

PLASMA THYROXINE (T_4) CONCENTRATIONS OVER TIME FOLLOWING EITHER AN INTRAPERITONEAL INJECTION OF 200 μg/kg NICOTINE HYDROGEN TARTRATE OR SALINE

Time (min)	Plasma T_4 (μg l^{-1}) (mean ± s.e.) Nicotine	Saline	Unpaired *t*-test, $p >$
0	53 ± 2	55 ± 2	0.05
5	47 ± 1	47 ± 2	0.05
10	57 ± 2	59 ± 2	0.05
15	53 ± 1	54 ± 1	0.05
20	60 ± 3	57 ± 2	0.05
30	55 ± 2	58 ± 4	0.05
45	53 ± 2	53 ± 1	0.05
60	51 ± 2	54 ± 1	0.05
120	53 ± 2	53 ± 1	0.05
6 hr	50 ± 3	52 ± 1	0.05
24 hr	53 ± 2	56 ± 2	0.05

low cross-reactivity with L-thyroxine (0.2%) 3,5-diiodo L-thyronine (0.5%) 3,5-diiodo-L-tyrosine (0.1%) and 3-iodo-L-tyrosine (0.1%). The anti-T4 serum had the following percentage cross-reactivity: L-triiodothyronine (5%) D-thyroxine (90–110%), 3,5-diiodo-L-tyrosine (0.5%) and 3-iodo-L-tyrosine (0.5%). Thyroxine binding globulin blocking agent, thiomersalate, allowed total serum T_3 and T_4 to be assayed directly without preliminary extraction. In the case of both T_3 and T_4 the sensitivity of the assay was found to be approximately 0.05 μg l^{-1} with a reproducibility of 4%. Radioactivity was determined by an automated gamma counter (Packard 5320).

Corticosterone Assay

Corticosterone was assayed by the competitive protein binding assay as described by Murphy [11]. Corticosterone was extracted with dichloromethane. Lypholysed human serum (Q-Pak Hyland control serum, Travenol Laboratories) was used as binding protein. Unbound 1,2,^{3}H-corticosterone (New England Nuclear) was removed using florisil. The sensitivity of the assay was 20 μg l^{-1} and the inter and intra assay variability was 4.6 and 4.0% respectively.

Procedure

To eliminate the stress of handling and injection, which might influence the normal functioning of the thyroid, animals were habituated to an intraperitoneal injection of physiological saline for 5 days prior to experimentation. Animals were subsequently administered with either 200 μg kg $^{-1}$ nicotine hydrogen tartrate or saline and sacrificed (in groups of 8 animals) at 0, 5, 10, 15, 20, 30, 45, 60 min and 2, 6 and 24 hr following an initial injection of nicotine. Blood was collected by exsanguination and the cell free plasma divided into four aliquots , for T_3, T_4, and corticosterone determinations.

RESULTS

The results for Plasma T_3 and T_4 levels after the administration of nicotine or saline are presented in Tables 1 and 2.

TABLE 3

PLASMA CORTICOSTERONE CONCENTRATIONS OVER TIME FOLLOWING EITHER AN INTRAPERITONEAL INJECTION OF THE 200 μg/kg NICOTINE HYDROGEN TARTRATE OR SALINE

Time (min)	Plasma corticosterone (μg l^{-1}) (mean ± s.e.) Nicotine	Saline	Unpaired *t*-test *p*
0	236 ± 23	241 ± 30	>0.05
5	354 ± 43	210 ± 41	<0.05
10	391 ± 64	249 ± 30	<0.05
15	398 ± 48	241 ± 41	<0.05
20	665 ± 64	216 ± 28	<0.001
30	429 ± 30	208 ± 25	<0.001
45	365 ± 68	235 ± 40	<0.05
60	218 ± 28	209 ± 37	>0.05
120	174 ± 19	169 ± 44	>0.05

These data indicate no significant change in either the T_3, $F(10,77)=0.31$, $p>0.05$, or T_4 concentrations, $F(10,77)=0.57$, $p>0.05$, with this dose of nicotine over the time period examined.

Plasma corticosterone levels following the administration of nicotine or saline are shown in Table 3. It can be seen that after 5 min there is a significant elevation in plasma corticosterone in the nicotine group (unpaired *t*-test; $p<0.05$). This significant elevation in corticosterone continues through to 45 min. There is no significant difference between the levels of corticosterone in the nicotine and saline groups at 60 and 120 min ($p>0.05$).

DISCUSSION

Most of the work on nicotine's action on thyroid function has involved indirect measurement of thyroid activity, and

has resulted in a degree of confusion. Histological evidence using thyroids from chronically nicotine treated animals has suggested everything from elevated thyroid activity to degeneration and hypofunction (see Introduction). Strauss [14] reported an increased secretion of thyroid hormone in rabbits and dogs after 2 to 4 months of daily nicotine administration and in human smokers after several days of nicotine administration. Similarly, Gutzeit and Parade [6] found that stimulation with nicotine in non-smokers caused a rise in total blood iodine with the greatest increase appearing in the organic iodine content, normally indicative of thyroid secretion. However nicotine has been found to have no effect on plasma TSH levels over a 60 min period in female rats [1]. In the present study nicotine did not alter the plasma levels of either thyroid hormone (T_3 or T_4), although it did produce a significant increase in plasma corticosterone.

Ingbar [7] noted an increased urinary disposal of inorganic idoine in rats subjected to glucocorticoid administration, suggesting that an elevation in glucocorticoid levels may have a positive effect on thyroid activity. In most stress situations both thyroid gland and adrenal cortex are stimulated simultaneously [9,12]. However, there are other reports which shown that an inverse relationship may exist between the adrenal cortex and thyroid gland, a stimulation of one axis correlating with a suppression of the other [5,13]. Such a relationship was not seen following nicotine administration, the increase in plasma corticosterone was not associated with a change in thyroid hormone levels.

It would appear that, while acute administration of nicotine may influence activity and metabolism through its effects on the circulating levels of catecholamines, glucocorticoids and insulin, it does not appear to alter the levels of the thyroid hormones in the short term.

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