Note

Effects of Adrenalin on the Conversion Ratio of Tryptophan to Niacin in Rats

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The administration of glycemia-affecting chemicals such as alloxan, streptozotocin, and 6-aminonicotinamide decreases the conversion ratio of tryptophan to niacin. Adrenalin is also known to increase the glucose level. For this reason, the effects of adrenalin on the conversion ratio were investigated. We found that the conversion ratio of tryptophan to niacin was reduced to half by the intraperitoneal injection of adrenalin at 75 μg/day/rat (body weight, about 250 g) every day for 7 days. Niacin decreases adrenalin-stimulated glycogenolysis via stimulating phosphodiesterase activity or depressing adenylyl cyclase activity. Accordingly, in urgent need of energy, animals would have to decrease the concentration of niacin within the body.

Adrenalectomy decreases the ACMSDase activity, a key enzyme in the conversion pathway of Trp to niacin. In rats, an

Table Effects of Intraperitoneal Injection of Adrenalin on the Body Weight, Food Intake, and Food Efficiency Ratio

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Adrenalin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial body weight (g)</td>
<td>224 ± 3</td>
<td>224 ± 5</td>
</tr>
<tr>
<td>Final body weight (g)</td>
<td>258 ± 6</td>
<td>245 ± 8</td>
</tr>
<tr>
<td>Gain in body weight (g/7 days)</td>
<td>34 ± 4</td>
<td>21 ± 4*</td>
</tr>
<tr>
<td>Food intake (g/7 days)</td>
<td>125 ± 5</td>
<td>101 ± 5*</td>
</tr>
<tr>
<td>Food efficiency ratio*</td>
<td>0.27 ± 0.02</td>
<td>0.20 ± 0.03*</td>
</tr>
</tbody>
</table>

* Body weight gain/food intake (g/g) through 7 days. Values are means ± SEM for five rats.

Fig. 1. Effects of Adrenalin on the Urinary Excretion of Nam (A), MNA (B), 2-Py (C), and 4-Py (D).

○, control; ●, adrenalin. Each point and bar represents the mean ± SEM for five rats.

*Significantly different at p < 0.01 compared with control group on the same measured day, as evaluated by Student's t test.

Abbreviations: Trp, tryptophan; Nam, nicotinamide; NiA, nicotinic acid; ACMSDase, aminocarboxymuconate-semialdehyde decarboxylase; NEFA, non-esterified fatty acids; XA, xanthurenic acid; KA, kynurenic acid; ANA, anthranilic acid; 3-HA, 3-hydroxyanthranilic acid; MNA, N1-methylnicotinamide; 2-Py, N1-methyl-2-pyridone-5-carboxamide; 4-Py, N1-methyl-4-pyridone-3-carboxamide; FER, food efficiency ratio.
injection of prednisolone, a synthetic adrenal cortex hormone, increases the activity of ACMSDase and decreases the conversion ratio. A reverse relationship has been proposed to hold between the ACMSDase activity and the conversion ratio of Trp to niacin. Adrenal hormones are considered to decrease the conversion ratio, but the effect of an adrenal medulla hormone, adrenalin, on the conversion has not yet been reported. In this experiment, the effects of adrenalin on the conversion ratio of Trp to niacin were investigated.

Nam and ANA were purchased from Wako Pure Chemical Industries (Osaka, Japan). MNA chloride, XA, KA, and 3-HA were obtained from Tokyo Kasei Kogyo (Tokyo, Japan). 2-Py and 4-Py were synthesized by the methods of Pullman and Colowick and Shibata et al. All other chemicals used were of the highest purity available from commercial sources.

Male rats of the Wistar strain (7 weeks old) were obtained from Clea Japan (Tokyo, Japan) and housed in metabolic cages (CT-10; Clea Japan). The rats which had been fed ad libitum for 7 days with a NiA-free, 20% casein diet, were intraperitoneally injected with 0.5 ml of sterilized saline once a day for 7 days to accustom them to the experimental conditions. Then, they were divided into two groups and fed ad libitum for 7 days more with the same diet. One group was intraperitoneally injected with 0.5 ml of saline alone every day during the period as a control, and the other was given with a 0.5 ml saline solution containing 75 μg of adrenalin. A significant decrease in the food intake was caused by injections of adrenalin. Concomitantly, the body weight gain in the adrenalin group was statistically significantly lower than that in the control group, as shown in the Table. FER was also statistically lower in the adrenalin group. The urine samples (09:00 a.m.-09:00 a.m.; 24-h urine) were periodically collected in amber bottles with 1 ml of 1 M HCl and stored at −25°C until needed. The rats were killed by decapitation after the last collection of urine samples had been finished. The liver of each animals was removed, and a portion of the liver (approximately 1 g) was treated as described in the literature to measure the ACMSDase (EC 4.1.1.45), a key enzyme in the metabolism of Trp to niacin. The measurement of this enzyme was done by the method of Ichiyama et al.

To calculate the conversion ratio of Trp to niacin, the urinary contents of Nam, MNA, 2-Py, and 4-Py were measured by HPLC. The conversion ratio was calculated as the sum of the urinary excretion of Nam + MNA + 2-Py + 4-Py (μmol/day) × 100/Trp intake (μmol/day).

The urinary contents of KA, XA, ANA, and 3-HA were similarly measured using the urine collected on the last day of the experiment.

No significant difference was observed between the two groups for the contents of the upper intermediates of such Trp metabolites as KA, ANA, XA, and 3-HA in the urine. The periodical changes of the urinary excretion of Nam, MNA, 2-Py, and 4-Py are shown in Fig. 1. The urinary excretion of Nam was not different between the two groups during the experiment. On the contrary, the urinary excretion of MNA, 2-Py, and 4-Py each in the adrenalin group was statistically decreased. Therefore, the sum of the urinary excretion was significantly lower in the adrenalin group than in the control group, and the conversion ratio of Trp to niacin was significantly lower in the adrenalin group than in the control group, as shown in Fig. 2. From these findings, it was proved that adrenalin significantly decreased the conversion ratio of Trp to niacin and the adrenal cortex and medulla hormones both served as decreasing the conversion ratio of Trp to niacin. As mentioned above, adrenalecetomy decreases the ACMSDase activity, and in this experiment, this activity was significantly higher in the adrenalin group (2.21 ± 0.17; means ± SEM for five rats) than in the control group (1.35 ± 0.13).

![Fig. 2. Effects of Adrenalin on the Urinary Excretion of Sum (A) and the Conversion Ratio of Trp to Nam (B).](image)

The effects of oral adrenalin administration on the conversion were investigated. Rats were fed for 28 days with an NiA-free, 20% casein diet containing 0.002% adrenalin; nevertheless, nothing happened (data not shown). The reason is probably because that adrenalin was destroyed by an enzyme in the small intestine.

In any case, the administration of glycemia-affecting chemicals such as alloxan, streptozotocin, and 6-aminonicotinamide to rats decreases the conversion ratio of Trp to niacin. Additionally, it has been reported that niacin decreases adrenalin-stimulated glycogenolysis via stimulating phosphodiesterase activity or depressing adenyl cyclase activity. Accordingly, in urgent need of energy, it would have to decrease the concentration of niacin. It thus seems reasonable that Trp is more apt to be metabolized into the production of acetyl-CoA (energy formation) than into the niacin formation.

References

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