EFFECT OF TAURINE ON ALTERATION IN ADRENAL FUNCTIONS INDUCED BY STRESS

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Abstract—When rats were exposed to immobilized cold stress, adrenaline content in the adrenal gland as well as noradrenaline content in the brain stem were reduced drastically, while noradrenaline content in the atria was not altered by the application of stress. Oral administrations of taurine (4-7 g/kg/day, for 3 days) prevented the stress-induced decline of adrenaline in the adrenal gland and this preventive effect could not be duplicated by the administration of L-isoleucine or DL-methionine. In hypophysectomized rats, the stress also induced a significant fall in adrenaline content of the adrenal gland, however taurine administration did not show significant preventive effects on the decline in adrenal catecholamines. The immobilized cold stress induced a significant increase in blood sugar and this increase was antagonized by pretreatment with taurine. Taurine had no significant effects on the stress-induced increase in the activity of adrenal tyrosine hydroxylase and the turnover rate of adrenaline in the adrenal gland measured by the rate of decline of this amine following p-methyl-tyrosine administration. The administration of taurine, in both in vivo and in vitro, inhibited the release of adrenaline from adrenal medullary granules, but that of dopamine-β-hydroxylase was not significantly affected. The stress-induced elevation of the blood level of corticosterone was not affected by taurine administration. These findings indicate that taurine antagonizes the stress-induced elevation of blood sugar by reducing adrenaline output from the adrenal gland. The regulatory mechanism most likely involves the inhibition of adrenaline release from adrenal medullary granules, possibly by stabilizing the membrane of the granules.

Numerous reports have shown that taurine (2-aminoethanesulfonic acid) inhibits the transmission of nerve impulses in a variety of mammalian and non-mammalian test preparations (1-5). In addition, antagonistic effects of this compound against ouabain-induced (6) and cobalt-induced (7) seizures have been reported. On the other hand, a number of studies have demonstrated that urinary excretion of taurine is modified by the administration of ACTH (8, 9) or glucocorticoids (8, 10), and on the contrary taurine has a regulatory role in hormone secretion by varying the pituitary activity (11).

In this study, we investigated the effect of taurine on the alteration of adrenal functions induced by immobilized stress in rats, with particular references to the effect on stress-induced alterations in the catecholamine release from the adrenal medulla.

MATERIALS AND METHODS

Animal care: Male Wistar rats weighing 200-250 g were used throughout and were fasted for 20 hr before each experiment. Hypophysectomized rats were used 2 weeks after the operation. For the administration of various amino acids (taurine, L-isoleucine, and
DL-methionine), each amino acid was dissolved in drinking water (3% w/v) and provided *ad libitum* for 3 days. Average daily dose of each amino acid ingested was 4-7 g/kg. Under the same experimental conditions, control animals were provided drinking water without the addition of any of these amino acids.

For the application of immobilized cold stress, a modified method of Takagi and Okabe (42) was used. The animals were fasted for 20 hr, then confined for 3 hr in a metallic restraint cage which was immersed into water up to the xiphoid process and which was kept at 20°C. **Chemical and enzymatic assays**

*Assay of catecholamines:* After decapitation, brain stem (diencephalon, mesencephalon, pons and medulla oblongata), atria and adrenal glands were rapidly removed and adrenaline (Ad) and noradrenaline (NAd) in these tissues were extracted according to the procedure of Chang (12). Ad and NAd were measured fluorometrically by the method of Häggendal (13). The same Ad assay method was also employed for experiments measuring Ad release.

*Measurements of adrenaline release:* For the preparation of chromaffin granules from the adrenal glands, the medullae were mechanically depressed and gently homogenized (0°C) in Locke's solution containing 10 μM iproniazid (2 medullae/ml), and the granules were fractionated from the homogenate by a 2-layered centrifugation procedure described by Greenberg and Sabelli (14). The supernatant layer containing sedimentable chromaffin granules was incubated at 30°C for 20 min. In some experiments, various concentrations of taurine were added in vitro to the supernatant layer obtained from control animals. After various incubations, the mixture was layered over with 0.5 M sucrose and centrifuged at 20,000 g for 20 min at 0°C to obtain a pellet form of the granules. Ad content in both the pellet and supernatant were measured and the rate of release in each sample was expressed by the percent of Ad retained in the pellet to the rates in both the supernatant and pellet fractions.

*Measurements of tyrosine hydroxylase activity:* Tyrosine hydroxylase activity was measured according to the method of Nagatsu et al. (1964) (15). Adrenal glands were homogenized with 3 vol. of 0.32 M sucrose containing 1 mM 2-mercaptoethanol. The incubation medium consisted of 400 μmoles of acetate buffer (pH 6.0); 200 μmoles of 2-mercaptoethanol, 2 μmoles of FeSO₄, 2 μmoles of L-6-methyltetrahydropterine HCl, 0.5 ml of enzyme preparation in a final volume of 2 ml. The reaction was initiated by adding 0.05 μCi of tyrosine-2-C¹⁴ (S.A.: 40.5 mCi/mmole) and terminated by adding 4 ml of 5% trichloroacetic acid and 20 μg of L-Dopa. The incubation was carried out at 37°C for 20 min and Dopa-C¹⁴ formed was separated by an alumina column. The radioactivity was measured using a Packard Tri-carb scintillation spectrometer Model 3390.

*Measurement of dopamine-β-hydroxylase activity:* Dopamine β-hydroxylase (DBH) activity was measured by the method of Creveling et al. (1962) (16). The incubation medium (final volume; 1 ml) contained 1 M phosphate buffer (pH 5.5), 0.2 M disodium fumarate, 0.2 M ascorbic acid, 0.2 M N-ethylmaleimide, catalase (1,500 unit, Sigma C-100), 0.1 M tyramine, 0.02 M pargyline and 1 mg protein of the water homogenate of adrenal glands as an enzyme preparation. Incubations were carried out at 37°C for 90 min and the reaction
was terminated by adding 0.2 ml of 3 M trichloroacetic acid. After the centrifugation, 1 ml of supernatant was applied to a Dowex-50-8X (H⁺ form) column (0.5 cm). The column was washed with 10 ml of water and octopamine converted from tyramine was eluted with 3 ml of 3 N NH₄OH. Octopamine in the elute was converted to p-hydroxybenzaldehyde by the addition of 0.3 ml of 2% sodium periodate and excess periodate was reduced with 0.3 ml of 10% sodium metabisulfite. The optical density was measured at 330 nm and activity was calculated by comparing with the same octopamine standard carried through the entire procedure.

Determinations of blood sugar and corticosterone levels in blood plasma, and protein:
Blood sugar levels were measured by the method of Hagedorn and Jensen (17). Unconjugated corticosterone in plasma was assayed fluorometrically by the method of Glick et al. (18) after extracting with isooctane and chloroform. Protein content was determined spectrophotometrically by the method of Lowry et al. (19). Taurine contents in various organs were assayed by the use of an amino acid analyzer after extracting taurine with 5% TCA. For the determination of blood levels of taurine, blood serum was used directly.

RESULTS
Effect of taurine on stress-induced alterations of catecholamine contents in atria, adrenal gland and brain stem

Alterations in catecholamine contents in the atria, adrenal gland and brain stem under the application of immobilized stresses and the effects of oral administration of various amino acids on the stress-induced changes in catecholamine contents are summarized in Table 1. By the application of immobilized cold stress for 3 hr, the adrenaline content in the adrenal

<table>
<thead>
<tr>
<th>Stress</th>
<th>Atria NAd(µg/g) ± S.E.M.</th>
<th>Adrenal gland Ad(µg/g) ± S.E.M.</th>
<th>Brain stem NAd(ng/g) ± S.E.M.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>2.10 ± 0.19</td>
<td>781 ± 94</td>
<td>636 ± 24</td>
</tr>
<tr>
<td>Taurine</td>
<td>2.31 ± 0.24</td>
<td>366 ± 55*</td>
<td>364 ± 22**</td>
</tr>
<tr>
<td>L-Isoleucine</td>
<td>2.25 ± 0.03</td>
<td>710 ± 77</td>
<td>608 ± 68</td>
</tr>
<tr>
<td>DL-Methionine</td>
<td>1.78 ± 0.10</td>
<td>650 ± 44</td>
<td>393 ± 25**</td>
</tr>
<tr>
<td></td>
<td>1.76 ± 0.20</td>
<td>744 ± 48</td>
<td>524 ± 74</td>
</tr>
<tr>
<td></td>
<td>1.39 ± 0.05</td>
<td>453 ± 61</td>
<td>378 ± 50**</td>
</tr>
<tr>
<td></td>
<td>1.64 ± 0.15</td>
<td>484 ± 53*</td>
<td>361 ± 69**</td>
</tr>
</tbody>
</table>

Mean ± S.E.M. obtained from 4 separate experiments.
* p<0.01, ** p<0.05, compared with non stressed control animals.
Each amino acid was given orally, 4-7 g/kg/day for 3 days.
a) Average taurine contents at the time of sacrifice were as follows: Control animals: blood serum, 27 µmoles/L; heart, 39 µmoles/g; adrenal gland, 27 µmoles/g; Brain, 9 µmoles/g. Taurine treated animals: blood serum, 175 µmoles/L; heart, 53 µmoles/g; adrenal gland, 40 µmoles/g; Brain, 13 µmoles/g, respectively.
gland as well as noradrenaline content in the brain stem, major catecholamines present in these organs respectively, were reduced significantly, whereas noradrenaline content in the cardiac atria remained unchanged. The oral administration of taurine (4–7 g/kg/day for 3 days) abolished completely the stress-induced decrease in adrenaline content of the adrenal gland, whereas the decrease of noradrenaline in the brain stem was not prevented with taurine administration. This lack of preventive effect of taurine in the stress-induced noradrenaline reduction in the brain stem may be a reflection of low penetrability of taurine into the brain, possibly due to the presence of blood-brain barrier. In fact, little increase in taurine level in the brain was noted following the oral administration of taurine (Table 1). In contrast with the significant preventive effect of taurine on the stress-induced decrease in adrenaline content of the adrenal gland, not only L-isoleucine, but also DL-methionine, a sulphur containing and metabolically related amino acid, had no antagonistic effect on the adrenaline reduction. These results clearly indicate that taurine has a specific preventive effect on stress-induced reduction of adrenaline in the adrenal gland. Since it is generally considered that physiological responses induced by the application of stress may be, at least in part, due to activations of the pituitary-adrenal axis, we examined the effect of hypophysectomy on the preventive effect of taurine on the stress-induced decrease in adrenaline content of the adrenal gland, atria and brain stem (Table 2). In hypophysectomized rats, noradrenaline contents in both atria and brain stem were reduced drastically, whereas adrenaline content in the adrenal gland expressed per g wet weight showed a significant increase. Since the activity of phenylethanolamine-N-methyltransferase, the enzyme catalyzing the formation of adrenaline by N-methylation of noradrenaline, is depressed following hypophysectomy (20), the increase of adrenaline which occurred in the adrenal gland could not be explained by the increase of adrenaline synthesis but may be a reflection of a decrease in the adrenal weight. In fact the weight of adrenal glands in hypophysectomized rats was less than one third of that found in control animals and adrenaline content per adrenal gland also showed a drastic decrease. In these hypophysectomized animals,

<table>
<thead>
<tr>
<th>stress</th>
<th>Atria NAd(g/g) ± S.E.M.</th>
<th>Adrenal gland Ad(g/g) ± S.E.M.</th>
<th>Brain stem NaAd(ng/g) ± S.E.M.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>1.22 ± 0.12 (4)</td>
<td>1184 ± 129 (6)</td>
<td>461 ± 32 (4)</td>
</tr>
<tr>
<td>Taurine treated</td>
<td>1.31 ± 0.14 (4)</td>
<td>577 ± 76 (6)</td>
<td>303 ± 25* (4)</td>
</tr>
<tr>
<td></td>
<td>1.75 ± 0.29 (4)</td>
<td>1382 ± 85 (4)</td>
<td>461 ± 17 (4)</td>
</tr>
<tr>
<td></td>
<td>1.17 ± 0.24 (4)</td>
<td>752 ± 169 (5)</td>
<td>247 ± 46+ (4)</td>
</tr>
</tbody>
</table>

* P < 0.01, compared with non stressed controls.
** P < 0.05, compared with non stressed controls.

Numbers in parentheses indicate the number of experiments.

Hypophysectomized rats were used 2 weeks after operation.

Taurine was given orally, 4–7 g/kg/day for 3 days.

Average weight of a pair of adrenal glands from hypophysectomized rats was 8 mg, whereas that from a non operated animals was 27 mg.
the application of stress also induced remarkable reductions in adrenaline content of the adrenal gland as well as in noradrenaline content of the brain stem. Under the same conditions, noradrenaline content of atria showed no significant changes. By contrast to the results obtained in non hypophysectomized rats, taurine had no significant preventive effects on stress-induced reduction of adrenaline content in the adrenal gland of hypophysectomized animals. These results suggest that the preventive effect of taurine on the reduction of adrenal catecholamine induced by the application of stress may occur, at least in part, because there is a change in the activity of pituitary gland as already suggested (11).

Effect of taurine on stress-induced increase in blood sugar

Table 3 shows the effect of taurine on changes in the levels of blood sugar induced by the application of stress. The immobilized cold stress induced a significant increase in blood sugar. The taurine administration suppressed this elevation of blood sugar induced by the stress, and this antagonistic effect of taurine was statistically significant. Since the patterns of changes in blood sugar (Table 3) and adrenaline content in the adrenal gland (Table 1) are similar in both control and taurine treated animals, the antagonistic effect of taurine on stress-induced increase in blood sugar is probably explainable as a reflection of the preventive effect of taurine on the increased outflow of adrenaline from the adrenal gland as a result of the stress.

**Table 3. Effect of oral administration of taurine on stress-induced alterations of blood sugar**

<table>
<thead>
<tr>
<th></th>
<th>Blood sugar (mg/dl)</th>
<th>S.E.M.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non stressed</td>
<td>Stressed</td>
</tr>
<tr>
<td>Control</td>
<td>76 ± 10 (4)</td>
<td>142 ± 3 (4)</td>
</tr>
<tr>
<td>Taurine treated</td>
<td>80 ± 15 (4)</td>
<td>121 ± 6 (4)*</td>
</tr>
</tbody>
</table>

* P<0.01, compared with each control group.
Numbers in parentheses indicate number of experiments.
Taurine was given orally, 4–7 g/kg/day for 3 days.

Effect of taurine on tyrosine hydroxylase activity and adrenaline turnover in the adrenal gland

It is well known that the metabolism of catecholamine in various organs is accelerated by the application of stress (21–23) and tyrosine hydroxylase, a rate limiting enzyme of catecholamine synthesis, also is inducible by the same procedure (24). Since a possibility exists that the antagonistic effect of taurine observed with the stress-induced decrease of adrenaline content in the adrenal gland may be due to the activation of tyrosine hydroxylase activity and/or the change in catecholamine turnover in this organ, we examined the effect of taurine on these parameters. As shown in Table 4, the application of immobilized cold stress significantly increased tyrosine hydroxylase activity, however the administration of taurine did not modify at all these increases induced by the stress. In addition, the rate
TABLE 4. Effect of oral administration of taurine on tyrosine hydroxylase activity and adrenaline content in adrenal glands after tyrosine hydroxylase inhibition following administration of α-methyl tyrosine (αMT)

<table>
<thead>
<tr>
<th>Stress</th>
<th>Tyrosine hydroxylase activity (nmoles/g w.w/hr) ± S.E.M.</th>
<th>Adrenaline Content (µg/g) ± S.E.M.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>7.3±1.1 (6)</td>
<td>Control 781±94 (4)</td>
</tr>
<tr>
<td></td>
<td>11.5±2.2 (4)**</td>
<td>374±27 (4)</td>
</tr>
<tr>
<td>Taurine treated</td>
<td>9.1±1.1 (5)</td>
<td>Turine treated 710±77 (4)</td>
</tr>
</tbody>
</table>
|         | 12.8±1.5 (4)**                                         | 347±32 (4)                       | 363

** P<0.05, compared with non stressed controls.
Numbers in parentheses indicate number of experiments.

- a) Measured 6 hr after the administration of α-methyl tyrosine (αMT, 200 mg/kg, i.p.), a tyrosine hydroxylase inhibitor.
- b) Taurine was given orally in a dose of 4–7 g/kg/day for 3 days.
- c) Calculated from the difference with and without αMT administration.

Effect of taurine on the adrenaline release from adrenal medullary granules and Dopamine-β-hydroxylase (DBH) activity in the adrenal gland

It has been reported that catecholamine in chromaffin granules of the adrenal medulla is released in vitro (14, 25). We studied the effect of taurine administration, in both in vitro and in vivo, on the release of adrenaline from adrenal medullary granules. As shown in Table 5, taurine administered both in vivo and in vitro inhibited the spontaneous release

TABLE 5. Effect of taurine administration on adrenaline (Ad) release from adrenal medullary granules

<table>
<thead>
<tr>
<th>Adrenaline % retained ± S.E.M.</th>
<th>A) In vivo</th>
<th>Taurine added (mM)</th>
<th>B) In vitro</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>40.7±2.7</td>
<td>—</td>
<td>44.7±4.1</td>
</tr>
<tr>
<td>Taurine treated</td>
<td>56.6±2.1**</td>
<td>1.0</td>
<td>52.9±3.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.0</td>
<td>56.2±3.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10.0</td>
<td>56.3±1.4**</td>
</tr>
</tbody>
</table>

Mean ± S.E.M. obtained from 4 separate experiments.
** P<0.05, compared with each control.
§ calculated by the following equation:

Ad in pellet (µg/g.w.w.) × 100

Ad in pellet (µg/g.w.w.) + Ad in supernatant(µg/g.w.w.)

Taurine was given orally, 4–7 g/kg/day for 3 days.
TAURINE AND STRESS ON ADRENAL FUNCTIONS

Table 6. Effect of oral administration of taurine on stress-induced alterations of dopamine-β-hydroxylase (DBH) activity in the adrenal gland

<table>
<thead>
<tr>
<th>Stress</th>
<th>DBH activity (pmol/mg pr/min) ± S.E.M.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>- 305 ± 83</td>
</tr>
<tr>
<td></td>
<td>+ 173 ± 10*</td>
</tr>
<tr>
<td>Taurine treated</td>
<td>- 244 ± 16</td>
</tr>
<tr>
<td></td>
<td>+ 183 ± 58</td>
</tr>
</tbody>
</table>

Mean ± S.E.M. obtained from 4 separate experiments.

* P < 0.01, compared with non-stressed controls.

Taurine was given orally, 4-7 g/kg/day for 3 days.

Table 7. Effect of oral administration of taurine on stress-induced alterations in the blood level of corticosterone

<table>
<thead>
<tr>
<th>Stress</th>
<th>Corticosterone in plasma (μg/dl) ± S.E.M.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>- 44.6 ± 3.5</td>
</tr>
<tr>
<td></td>
<td>+ 69.8 ± 3.4*</td>
</tr>
<tr>
<td>Taurine treated</td>
<td>- 53.4 ± 2.2</td>
</tr>
<tr>
<td></td>
<td>+ 76.7 ± 2.8*</td>
</tr>
</tbody>
</table>

* P < 0.01, compared with non-stressed controls.

Mean ± S.E.M. obtained from 4 separate determinations.

Taurine was given orally, 4-7 g/kg/day for 3 days.

of adrenaline and increased significantly the adrenaline retained in adrenal medullary granules. Exocytosis has been proposed as the mechanism by which the release of noradrenaline occurs from the sympathetic nerve following electrical stimulation (26, 27). Since it is generally considered that the discharge of noradrenaline by the exocytosis couples with that of dopamine-β-hydroxylase, ATP and chromogranin A, we studied the effect of taurine on stress-induced alterations of dopamine-β-hydroxylase activity in the adrenal gland. The application of stress induced significant decline in dopamine-β-hydroxylase activity in the adrenal gland, but the treatment of rats with taurine had no significant preventive effects on the decline of dopamine-β-hydroxylase activity (Table 6).

Effect of taurine on the stress-induced alterations of blood level of corticosterone

Immobilized stress induced significant increase in the plasma corticosterone, a major corticosteroid in the rat, but taurine administration had no significant preventive effects on the increase of plasma corticosterone induced by the stress (Table 7).

DISCUSSION

One of the interesting findings in this study is that oral administration of taurine antagonizes drastically the stress-induced decline of adrenaline in the adrenal gland and thus sup-
presses the elevation of blood sugar by the application of stress (Tables 1 and 3). It is well known that methionine is a precursor of taurine biosynthesis (28), however this preventive effect of taurine could not be duplicated by methionine administration. These results suggest that the preventive effect of taurine on stress-induced decline of adrenaline in the adrenal gland may be a rather specific phenomenon requiring a relatively high concentration of taurine at the target organ. In fact, taurine content in the adrenal gland increased by 48% following the oral administration of taurine. Considering the rapid uptake and turnover rate ($T_{1/2} = 1$ day) in the adrenal gland in comparison with those in brain and heart (29), a possible biosynthetic supply of taurine from administered methionine may not be great enough to prevent the stress-induced decline of the adrenaline in the adrenal gland.

The suppressive effects of taurine on stress-induced decline of adrenaline in the adrenal gland could not be detected when hypophysectomized rats were subjected to the same experimental procedures. It has been reported that hypophysectomy does not affect the endogenous level of taurine in various organs (30). Furthermore a large amount of taurine was given over the 3 day period. These facts suggest that the elimination of preventive effects of taurine on stress-induced decline of adrenal catecholamine may not be attributed to the changes in taurine concentration. Although regulatory roles of the hypophysis in the preventive effect of taurine on the decline of adrenal catecholamine are unclear at present, it may be that taurine suppresses the adrenaline release from adrenal medullary granules (Table 5), but recovery processes of adrenaline in the granules following the stress-induced discharge of this amine are retarded in hypophysectomized animals. In fact it has been reported that hypophysectomy reduces significantly the activities of both tyrosine hydroxylase and phenylethanolamine N-methyltransferase in the adrenal gland (20).

In contrast with significant preventive effects in the adrenal gland, the lack of preventive effect of taurine on the stress-induced decline of noradrenaline in the brain stem was noted (Table 1). It has been reported that systematically administered taurine can be found in the brain (31), but the extent of distribution is rather small, possibly due to the presence of the blood-brain barrier. The lack of preventative effect of taurine in the brain stem is most likely due to the lack of an adequate level of taurine for preventing stress-induced noradrenaline release. In our work, we have found little evidence of an increase in the brain level of taurine following taurine administration (Table 1).

To determine the mechanisms of preventive effect of taurine on the stress-induced decline of adrenaline in the adrenal gland, we examined the effect of taurine on the release of adrenaline from adrenal medullary granules, and on the tyrosine hydroxylase activity, the rate limiting enzyme in catecholamine synthesis (32), as well as catecholamine turnover in the adrenal gland. Oral administration of taurine did not modify either the stress-induced increase of adrenal tyrosine hydroxylase activity or the decline of adrenaline following the administration of $\alpha$-methyltyrosine, a competitive inhibitor of tyrosine hydroxylase (15). These results indicate that the preventive effects of taurine on the stress-induced decline in adrenaline content are not due to a facilitation of catecholamine biosynthesis and/or suppression of the turnover of adrenaline in this organ (Table 4).
On the other hand, taurine administration both in vivo and in vitro inhibited the adrenaline release from adrenal medullary granules (Table 5). This phenomenon is most likely related to the preventive effects of taurine on the stress-induced decline of adrenaline in the adrenal gland. In the process of exocytosis by which the secretion of catecholamine occurs from sympathetic nerve (26, 27), it is generally considered that dopamine-β-hydroxylase is also discharged from the vesicles (26, 27, 33). The application of immobilized stress also induced a significant fall in adrenal dopamine-β-hydroxylase activity. The administration of taurine, however, did not show significant preventive effects on the decline of dopamine-β-hydroxylase activity (Table 6). It has been reported that amphetamine releases catecholamine from chromaffin tissue by both exocytosis and by direct interaction with chromaffin granules, whereas tyramine is considered to have only the latter effect (25). This differentiation was made by observing whether or not the changes in the release of dopamine-β-hydroxylase, protein and/or adenine nucleotides occurred simultaneously with those of catecholamines and a portion of the catecholamine release which couples with the release of dopamine-β-hydroxylase was assigned to exocytosis. In addition, differential effects of a high dose of reserpine on the releases of catecholamine and dopamine-β-hydroxylase from the adrenal medullary storage vesicles (34) have been reported. It may thus be concluded that taurine prevents the catecholamine release from chromaffin tissue by direct interaction with chromaffin granules and has no significant effects on the process of exocytosis per se.

Taurine administration did not show significant effects on the stress-induced increase of the plasma level of corticosterone. It is well known that in most secretory organs, the secretory products are stored in granules or vesicles, and release occurs by exocytosis. In the adrenal cortex, however, the presence of such intracellular organelles responsible for the storage of corticosteroid was not detected morphologically (35, 36), and it has been reported that synthesized hormones diffuse out to the cell exterior (37, 38). These results suggest that the site of taurine action on the release of adrenal secretory products may be primarily localized on storage granules, such as medullary granules for catecholamine.

In the adrenal medulla, calcium plays important roles in "stimulus-secretion coupling" due to its properties to form stable complexes with various constituents (41) and affects membrane permeabilities. In this regard, it is of interest that taurine treatment increases calcium content in the heart as well as in liver mitochondria and the affinity of various cellular components for calcium (39, 40). If these facts are applicable to the adrenal medulla, the antagonistic effects of taurine on the stress-induced adrenaline release could be attributable to the increase of intragranular calcium, possibly by increasing the affinity of calcium to the medullary granular membrane and/or by decreasing the release of calcium from the granules. Experiments investigating such a possibility are underway in our laboratory.

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