CHANGES IN SERUM TSH LEVEL AFTER INTRAVENTRICULAR INJECTION OF VARIOUS NEUROMEDIATORS IN RATS

By

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ABSTRACT

The influence of various neuromediators on pituitary TSH secretion in rats has been investigated. Noradrenaline 50 μg/rat, dopamine 50 μg/rat, serotonin-creatinine-sulphate 100 μg/rat, gamma-aminobutyric acid 100 μg/rat, pilocarpine 1 mg/rat, histamine 100 μg/rat were administered into the lateral ventricle of the brain. All agents were dissolved in Parker's fluid. Two control groups of animals were given Parker's fluid and subjected to surgical manipulations, respectively. Plasma TSH level was estimated after 30 min by means of radioimmunoassay. The increase in the TSH level was observed after the injection of serotonin and noradrenaline (4.0 and 3.1 ng/ml, respectively) as compared with control group (0.7 ng/ml).

The influence of various neuromediators on pituitary thyrotrophin (TSH) secretion has been investigated mainly in dopaminergic and noradrenergic system (Refetoff et al. 1972; Spaulding et al. 1972; Rapaport et al. 1973; Tuomisto et al. 1975) as well as the serotoninergic system (Grimm & Reichlin 1973; Mess & Peter 1974, 1975).

The effect of various neuromediators on pituitary thyrotrophic function can be investigated in two ways. The indirect method consists in the intravenous injection of some drugs that influence either the neurohormone level or the functional condition of the appropriate receptor: they inhibit the synthesis or retard the disintegration of neuromediator, block or stimulate the receptor.
The direct way consists in the administration of the neuromediator itself. The procedure which sufficiently imitates the physiological conditions (Scott et al. 1974) is the injection of drugs into the lateral ventricle of the brain.

The effect of noradrenaline, serotonin, dopamine, gamma-aminobutyric acid, histamine and pilocarpine on TSH secretion was tested in our experiment.

MATERIAL AND METHODS

Forty-eight female Wistar rats of 100 ± 10 g body weight obtained from the Central Animal Farm in Zabrze were divided into 8 homogeneous groups (Table 1). The experiment was carried out at 3 p.m. in accordance with the circadian rhythm of TSH secretion (Panda & Turner 1967). The animals received intravenously 2 ml of 2% solution of chloralhydrate. The anaesthesia began 5 min before the experiment and creatinine-sulphate 100 µg/rat, gamma-aminobutyric acid 100 µg/rat, pilocarpine 1 mg/rat, histamine 100 µg/rat soluted in Parker's fluid were injected intraventricularly into the animals of respective groups. Two remaining groups were used as controls. One of them received intraventricularly the solvent, and another one was subjected to the surgical manipulations. The intraventricular injections in the amount of 30 µl were given with Hamilton's syringe by the method of Herman (1970) into the right ventricle of the brain. After 30 min the animals were decapitated and 1.5 ml blood samples were taken. The coagulated blood was centrifuged for 3 min at 6000 g. Serum TSH level was measured twice in each sample by means of the radioimmunological method with use of reagent kit produced by CEA-IRESORIN (sensitivity 0.02 ng). Scintillation counter Scale Timer PT 72 was used. The data obtained were elaborated statistically by means of double variance test and Duncan test (Weber 1957).

Table 1.

TSH level after intraventricular injection of neuromediators.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No. of rats</th>
<th>TSH level (ng/ml)</th>
<th>Standard error of mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control I (solvent only)</td>
<td>6</td>
<td>0.7</td>
<td>0.20</td>
</tr>
<tr>
<td>Control II (surgical manipulations)</td>
<td>6</td>
<td>0.75</td>
<td>0.11</td>
</tr>
<tr>
<td>Dopamine</td>
<td>6</td>
<td>0.75</td>
<td>0.25</td>
</tr>
<tr>
<td>Gamma-aminobutyric acid</td>
<td>6</td>
<td>1.1</td>
<td>0.12</td>
</tr>
<tr>
<td>Histamine</td>
<td>6</td>
<td>1.2</td>
<td>0.02</td>
</tr>
<tr>
<td>Pilocarpine</td>
<td>6</td>
<td>1.6</td>
<td>0.35</td>
</tr>
<tr>
<td>Serotonin</td>
<td>6</td>
<td>4.0</td>
<td>1.02*</td>
</tr>
<tr>
<td>Noradrenaline</td>
<td>6</td>
<td>3.1</td>
<td>1.01*</td>
</tr>
</tbody>
</table>

* Statistically significant difference in comparison with both control groups, P = 0.05.
RESULTS

The mean level of TSH in the first control group receiving solvent only was 0.7 ± 0.2 ng/ml (mean ± SEM); the second control group (surgical manipulations) showed similar TSH values 0.75 ± 0.1 ng/ml. Similar results were obtained in rats treated with dopamine, gamma-aminobutyric acid, histamine and pilocarpine (Table 1). Statistically significant increase of TSH level was observed after the injection of serotonin and noradrenaline 4.0 ± 1.0 and 3.1 ± 1.0 ng/ml, respectively. The difference between the two groups was not significant.

DISCUSSION

Reports concerning the influence of various neuromediators on TSH level differ considerably from each other. The increased serum TSH level after noradrenaline injection obtained in our experiment confirms the results obtained by Grimm & Reichlin (1973), who showed the stimulating effect of noradrenaline on thyrotrophin releasing hormone (TRH) release from mouse hypothalamus in vitro. Harrison (1961) reported that noradrenaline introduced into the hypothalamus or third ventricle did not change the activity of the hypothalamus-hypophysis-thyroid gland axis. However, this experiment was carried out by means of 131I release method (T/S ratio was also estimated) and these methods were probably not sensitive enough to demonstrate the subtle changes in TSH secretion. Tuomisto et al. (1975) confirm the stimulatory influence of noradrenaline on TSH secretion (cold stress model).

The second mediator which caused a statistically significant increase in TSH level – serotonin – has been considered as a factor affecting TSH secretion. It has been demonstrated by Chen & Meites (1975) that the serotonin pre-cursor, 5-OH-tryptophan stimulates TSH secretion. Drugs causing a decrease in serotonin contents in the brain, such as chloramphenamine, reserpine and α-methyltyrosine bring about a decrease in TSH level. Tuomisto et al. (1975) found that p-chloro-phenyloalanine (PCPA), the inhibitor of serotonin synthesis, decreased the normal serum TSH level. This observation was confirmed by Shopsin et al. (1974). A decrease in TSH and TRH content in the hypophysis and hypothalamus, respectively, after 5-OH-tryptamine injection, as obtained by Mess & Peter (1974, 1975), may be due to the increase in their release. There are however, some investigations in vitro, which contradict the above observations. Grimm & Reichlin (1973) found an inhibition of TRH release from the hypothalamus after serotonin administration. On the contrary, earlier reports (Harrison 1961) suggested, that serotonin introduced into the third ventricle had no effect on the serum TSH level. A similar conclusion was drawn by Paracchi et al. (1975) who administered serotonin receptor in-
hbitors in man. Dopamine, histamine and gamma-aminobutyric acid in our experiment caused no changes in the TSH level. The literature data are wider only as to dopamine (Refetoff et al. 1972; Grimm & Reichlin 1973; Nilsson & Thorell 1974; Nilsson et al. 1975; Chen & Meites 1975; Tuomisto et al. 1975) but it is too early to draw definitive conclusions.

It would seem of interest to study the role of the cholinergic system in the regulation of TSH release. Earlier reports indicate that pilocarpine injected either intravenously or intraperitoneally has no influence on the TSH level (Chen & Meites 1975). It has been rarely suggested that cholinergic receptors plays a part in the regulation of TSH secretion (Harrison 1961; Kotani et al. 1973).

All the neuromediators used in our experiment were given in relatively high doses, since the purpose was to select these substances, which influence the TSH level after intraventricular injection. The results obtained indicate the need for further investigations on the role of serotonin and noradrenaline in the regulation of TSH secretion, with the use of several doses of the neuromediator at a lower, more physiological level.

REFERENCES

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