JOURNAL OF PHYSIOLOGY AND PHARMACOLOGY 1997, 48, 4, 813—823

J. CIOSEK, B. STEMPNIAK

THE INFLUENCE OF VASOPRESSIN OR OXYTOCIN ON THYROID-STIMULATING HORMONE AND THYROID HORMONES' CONCENTRATIONS IN BLOOD PLASMA OF EUTHYROID RATS*

Department of Pathophysiology, Medical University of Lodz, Lodz, Poland

The effects of arginine vasopressin (AVP) and oxytocin (OT) upon thyroid-stimulating hormone (TSH), free thyroxine (FT_4) and free triiodothyronine (FT_3) release were studied in euthyroid rats. Intracerebroventricular (i.c.v.) infusion of AVP in doses of 0.5 ng or 5 ng led to significant increases in plasma levels of TSH as well as FT_4 and FT_3. The effects of OT injected i.c.v. in similar doses were not consistent (there was no parallel between the changes of respective hormones plasma levels).
It may be concluded that vasopressin modulate the pituitary-thyroid system function; AVP is probably a physiological stimulator of TSH and thyroid hormones secretion.

K e y w o r d s: *Vasopressin, oxytocin, thyroid-stimulating hormone, thyroid hormones*

INTRODUCTION

The neurohypophysial hormones are synthesized by separate populations of magnocellular neurons, whose perikarya primarily occupy the supraoptic (SON) and paraventricular (PVN) nuclei of the hypothalamus, and whose axons terminate within the posterior lobe of the pituitary gland. On the other hand, vasopressinergic and oxytocinergic axons project to the median eminence where their terminals end in juxtaposition to hypophyseal portal capillaries (1, 2). The high concentrations of vasopressin and oxytocin in the hypophyseal portal blood (3) suggest the participation of these neurohormones in the release of anterior pituitary hormones. Similarly to hypothalamic relasing factors, arginine vasopressin (AVP) affects directly the anterior pituitary (4—6) where AVP-specific receptors have been identified (7). Indeed,

*) Conducted under Contract No. 502-11-247 with the Medical University of Lodz, Lodz, Poland.

in the anterior lobe of the pituitary gland, AVP acts by binding to V_{1b} receptors as a secretagogue for adrenocorticotropic hormone (8). As to the oxytocin (OT), its effects seem to be limited to controlling ACTH release in some instances only, e.g., during stress (9—11). Moreover, AVP was found to act similarly to thyrotropin-releasing hormone (TRH) in *in vitro* studies on bovine or rat anterior pituitary slices (12, 13). Other studies (6, 14, 15) do not suggest, however, any important role for AVP as a regulator of TSH release in humans.

Several radioimmunological and immunocytochemical studies confirm the presence of TRH as well as of pro-TRH mRNA in the hypothalamus and neurohypophysis (16—20) where the possibility of TRH participation in mechanism of AVP and OT release may be supposed (21—28).

The aim of present study was to investigate the possible AVP and OT influence on thyroid-stimulating hormone (TSH), free thyroxine (FT_4) and free triiodothyronine (FT_3) release in euthyroid rats.

MATERIAL AND METHODS

Animals

The experiments were carried out on a total of 80 adult male Wistar rats weighing 390—430 g. They were kept at a temperature of about +22°C and in regulated light-dark conditions (light from 6.00 a.m. to 8.00 p.m.). The animals received standard pelleted food and had free access to tap water.

Experimental design

The rats were divided into five groups: I — animals injected intracerebroventricularly (i.c.v.) with 5 µl of vehicle (0.15 M sodium chloride solution); II — animals treated with arginine vasopressin (AVP; [Arg^8]-VP, Peninsula Lab. Ltd., lot No 029463) dissolved in sterile saline and administered i.c.v. at a dose of 0.5 ng (i.e., 5 µl of solution) injected at a rate of 5 µl per 15 sec; III — animals treated with AVP, similarly dissolved and administered at a dose of 5 ng; IV — animals treated with oxytocin (OT; Peninsula Lab. Ltd., lot No 027179) dissolved in sterile saline and administered i.c.v. at a dose of 0.5 ng (i.e., 5 µl of solution), injected at a rate of 5 µl per 15 sec; V — animals treated with OT, similarly dissolved and administered at a dose of 5 ng.

Experimental procedure

The experiments were carried out between 9.00 and 11.00 a.m. On the day of experiment, all animals were anaesthesized by an intraperitoneal (i.p.) injection of 10% urethane (1.4 ml/100 g b.w.) and the intracerebroventricular cannula was implanted. The animals were immobilized in a simple stereotaxic apparatus as recommended by Noble *et al.* (29); a small hole was drilled in the

skull (1.5—2.0 mm laterally and 1.5—2.0 mm posteriorly to the crossing of the sagittal and coronal sutures). A simple stainless steel cannula (inner diameter 0.5 mm) was inserted into the left cerebral ventricle; its tip was 4.0 mm below the dorsal skull surface. The cannula was fixed to the skull with dental cement.

In a separate experimental group, the effectiveness of i.c.v. injections was verified by injecting of 10 µl 0.25 per cent trypan blue solution (one rat injected with trypan blue solution for every eight animals injected with drug solution or 0.15 M sodium cloride) and was found to be quite satisfactory, i.e., the dye was distributed in an uniform manner within the cerebral ventricles.

For subsequent collection of blood samples and intravenous (i.v.) reinfusions, the left external jugular vein was cannulated. Then the course of experiment for animals of groups A-C was as follows: i.c.v. injection of vehicle or hormonal (AVP or OT) solution and immediate (i.e., at the latest 10 sec after injection) collection of 1.0 ml blood; time "10" and "30": samples of 1.0 ml blood were collected 10 min and 30 min after i.c.v. injection respectively. The collected blood was centrifuged for 5 minutes (+4°C; relative centrifugal force of about 650 G i.e., 6380 m/sec^2), the plasma removed and preserved at −23°C in sealed glass vials until radioimmunoassayed. Each sediment (mainly erythrocytes) was resuspended in an equal volume of 7% dextran solution (Dekstran 70000, Polfa, Kutno, lot No 01290) and reinfused i.v. into the same donor animal a few minutes before the next blood sample was collected.

Radioimmunoassay (RIA)

Kits for TSH determination were obtained from Amersham International (Little Chalfont, UK; lot No 59B). As evaluated by the producer, cross reaction with rat TSH for anti-TSH antibodies was 100%; with rat TSH (NIH-RP2) it was 103%; with rat GH — 0.32%; with rat FSH < 0.02%; with rat LH < 0.19%; with rat PRL < 0.05% and with rat ACTH < 0.008%. The sensitivity of the assay procedure was 0.05 ng per tube with intra- and inter-assay coefficient of variation of 4.8% and 13.2%, respectively.

Free thyroxine (FT_4) and free triiodothyronine (FT_3) were determined in plasma by RIA using kits produced by Immunotech (Marseille, France; lot No 12722-95-03-1441 and lot No 12728-95-03-1441, respectively). As evaluated by the producer, cross reaction with L-thyroxine for anti-FT_4 monoclonal antibody was 100%; with D-thyroxine — 33%; with L-3,3′, 5-triiodothyronine (T_3) — 0.8% and with L-3,3′,5′-triiodothyronine (rT_3) — 10.2%. The sensitivity of the assay procedure was 0.4 pM per tube with intra- and inter-assay coefficient of variation of 5.03% and 5.21%, respectively. Cross reaction with L-3,3′,5-triiodothyronine (T_3) as well as with L-3,3′,5-triiodothyroacetic acid for anti-FT_3 monoclonal antibody was 100%; with L-3,3′, 5′-triiodothyronine (rT_3) — 0.03%; with L-thyroxine — 0.15% and with D-thyroxine — 0.07%. The sensitivity of the assay procedure was 0.5 pM per tube with intra and inter-assay coefficient of variation of 4.88% and 5.63%, respectively.

Statistical evaluation of the results

The concentrations of radioimmunoassayed hormones in the blood plasma were finally expressed in nanograms per millilitre for TSH and in picomols per liter for FT_4 as well as FT_3. Values are reported as the mean ± standard error of the mean (S.E.M.). Data were calculated by analysis of variance (ANOVA); if ANOVA revealed significant effects, post hoc analyses were done using D-Duncan test ($p < 0.05$ was considered to be statistically significant).

RESULTS

The vasopressin and oxytocin influence on thyroid stimulating hormone (TSH) concentration in blood plasma (Table 1).

The TSH level in plasma of control rats (i.e., treated i.c.v. with 0.15 M NaCl; group I) decreased after the first 10 minutes, then it remained quite unchanged at the 30-th minute of the experiment.

Table 1. The effect of i.c.v. injecting arginine vasopressin (AVP) or oxytocin (OT) on plasma TSH concentrations in euthyroid rats (in ng/mL). The results are the mean ± S.E.M. for the groups.

Groups of rats \ Subgroups (minutes)	time "0" (a)	time "10" (b)	time "30" (c)	Significance as estimated by ANOVA and D-Duncan's test	
				a versus b	a versus c
I: rats injected i.c.v. with 0.15 M NaCl (n = 15)	5.37 ± 0.19	4.80 ± 0.15	4.83 ± 0.22	$p < 0.05$	NS
II: rats treated i.c.v. with 0.5 ng AVP (n = 16)	4.99 ± 0.16	5.50 ± 0.13	6.20 ± 0.25	$p < 0.05$	$p < 0.01$
III: rats treated i.c.v. with 5 ng AVP (n = 16)	5.12 ± 0.16	6.11 ± 0.40	6.05 ± 0.12	$p < 0.05$	$p < 0.01$
IV: rats treated i.c.v. with 0.5 ng OT n = 17)	5.12 ± 0.26	5.49 ± 0.24	5.10 ± 0.14	NS	NS
V: rats treated i.c.v. with 5 ng OT (n = 16)	5.11 ± 0.25	4.33 ± 0.19	4.90 ± 0.15	$p < 0.05$	NS
Significance as estimated by ANOVA and D-Duncan's test					
I versus II	NS	$p < 0.01$	$p < 0.01$		
I versus III	NS	$p < 0.01$	$p < 0.01$		
I versus IV	NS	$p < 0.05$	NS		
I versus V	NS	NS	NS		

Number of animals in parentheses
NS — not significant

I.c.v. injection of 0.5 ng AVP (group II versus group I) was followed by an increased TSH concentrations in plasma at 10-th min (time "10": $p < 0.01$) and 30-th min (time "30": $p < 0.01$) of the experiment, when compared with respective subgroups of group I. Similarly, a single i.c.v. dose of 5.0 ng AVP (group III versus group I) was followed by a significant increase of TSH level in plasma at 10-th min (time "10": $p < 0.01$) and 30-th min (time "30": $p < 0.01$) of the experiment.

TSH concentration in blood plasma of animals treated i.c.v. with 0.5 ng OT (group IV versus group I) increased during first 10-th minutes (time "10": $p < 0.05$) and then it remained at similar level. I.c.v. administration of 5 ng OT (group V versus group I) did not cause any significant changes in plasma TSH concentration.

The vasopressin and oxytocin influence on free thyroxine (FT_4) concentration in blood plasma (Table 2).

After the single i.c.v. injection of 0.15 M sodium chloride solution to the control animals (group I) the FT_4 plasma concentration remained unchanged at the 10-th and 30-th min of the experiment.

Table 2. The effect of i.c.v. injections of arginine vasopressin (AVP) or oxytocin (OT) on FT_4 concentrations in blood plasma in euthyroid rats (in pM/L). The results are the mean ± S.E.M.

Groups of rats / Subgroups (minutes)	time "0" (a)	time "10" (b)	time "30" (c)	Significance as estimated by ANOVA and D-Duncan's test	
				a versus b	a versus c
I: rats injected i.c.v. with 0.15 M NaCl (n = 15)	29.80 ± 0.44	28.96 ± 1.15	27.30 ± 1.04	NS	NS
II: rats treated i.c.v. with 0.5 ng AVP (n = 16)	29.28 ± 0.76	33.00 ± 1.13	34.18 ± 0.19	$p < 0.01$	$p < 0.01$
III: rats treated i.c.v. with 5 ng AVP (n = 16)	27.61 ± 0.61	33.20 ± 1.80	31.20 ± 1.18	$p < 0.01$	$p < 0.05$
IV: rats treated i.c.v. with 0.5 ng OT (n = 17)	26.89 ± 0.45	25.90 ± 0.77	30.40 ± 0.90	NS	$p < 0.01$
V: rats treated i.c.v. with 5 ng OT (n = 16)	33.80 ± 1.22	29.80 ± 1.48	25.20 ± 1.03	NS	$p < 0.01$
Significance as estimated by ANOVA and D-Duncan's test					
I versus II	NS	$p < 0.05$	$p < 0.01$		
I versus III	$p < 0.05$	$p < 0.05$	$p < 0.05$		
I versus IV	$p < 0.01$	NS	$p < 0.05$		
I versus V	$p < 0.01$	NS	NS		

Number of animals in parentheses
NS — not significant

The i.c.v. injection of 0.5 ng AVP (group II as compared with group I) resulted in distinct increase of FT_4 concentration in plasma 10 min (time "10": $p < 0.05$) and 30 min (time "30": $p < 0.01$) after injection. I.c.v. injection of 5 ng AVP (group III as compared with group I) was followed by significant decrease of plasma FT_4 level at time "0" ($p < 0.05$) of the experiment. From then on (i.e., at 10-th and 30-th minute of experiment) the FT_4 plasma concentration raised distinctly (time "10": $p < 0.05$; time "30": $p < 0.05$).

The plasma FT_4 concentration of animals treated i.c.v. with 0.5 ng OT (group IV as compared with group I), after initial decrease (time "0": $p < 0.01$) was somewhat increased at 30-th min (time "30": $p < 0.05$). The single i.c.v. dose of 5 ng OT (group V as compared with group I) resulted in a distinct rise of FT_4 level in blood plasma at time "0" ($p < 0.01$).

The vasopressin and oxytocin influence on free triiodothyronine (FT_3) concentration in blood plasma (Table 3).

Table 3. The effect of i.c.v. injecting arginine vasopressin (AVP) or oxytocin (OT) on FT_3 concentrations in blood plasma in euthyroid rats (in pM/L). The results are the mean ± S.E.M.

Groups of rats \ Subgroups (minutes)	time "0" (a)	time "10" (b)	time "30" (c)	Significance as estimated by ANOVA and D-Duncan's test	
				a versus b	a versus c
I: rats injected i.c.v. with 0.15 M NaCl (n = 15)	9.57 ± 0.38	9.98 ± 0.30	8.33 ± 0.35	NS	$p < 0.05$
II: rats treated i.c.v. with 0.5 ng AVP (n = 16)	11.18 ± 0.48	10.40 ± 0.22	9.60 ± 0.42	NS	$p < 0.05$
III: rats treated i.c.v. with 5 ng AVP (n = 16)	12.88 ± 0.21	10.37 ± 0.18	11.57 ± 0.32	$p < 0.01$	$p < 0.05$
IV: rats treated i.c.v. with 0.5 ng OT (n = 17)	11.68 ± 0.08	9.33 ± 0.26	8.85 ± 0.22	$p < 0.01$	$p < 0.01$
V: rats treated i.c.v. with 5 ng OT (n = 16)	13.08 ± 0.12	9.70 ± 0.43	8.75 ± 0.34	$p < 0.01$	$p < 0.01$
Significance as estimated by ANOVA and D-Duncan's test					
I versus II	$p < 0.01$	NS	$p < 0.05$		
I versus III	$p < 0.01$	NS	$p < 0.01$		
I versus IV	$p < 0.01$	NS	NS		
I versus V	$p < 0.01$	NS	NS		

Number of animals in parentheses
NS — not significant

The FT_3 blood plasma concentration in animals treated i.c.v. with 0.15 M NaCl (group I) did not change at time "0" and "10" but decreased at 30-th min of the experiment.

I.c.v. administration of 0.5 ng AVP (group II as compared with group I) and 5 ng AVP (group III as compared with group I) was followed by a distinct rise of FT_3 concentration in plasma at time "0" ($p < 0.01$ for groups II and III) as well as at 30-th min ($p < 0.05$ and $p < 0.01$ for group II and III, respectively).

The i.c.v. injections of 0.5 ng OT (group IV versus group I) and 5 ng OT (group V versus group I) increased the plasma FT_3 level only at time "0" ($p < 0.01$) of the experiment.

DISCUSSION

The possible role of vasopressin or oxytocin in the release of anterior pituitary hormones

In addition to the release of vasopressin and oxytocin from the posterior pituitary into the circulating blood, it is now established that these peptides are released within the central nervous system where they act as neurotransmitters or neuromodulators in the processes quite different than their peripheral actions. Both neurohormones were also reported to be released at the median eminence into the portal vessels which reach the anterior pituitary (30).

The influence of vasopressin and oxytocin on the release of anterior pituitary hormones, including growth hormone (GH), thyroid-stimulating hormone (TSH) and prolactin still remains not clear. The earlier findings are not numerous and often contradictory. None the less, it has been reported that both vasopressin and corticotropin-releasing hormone (CRH) participate *in vivo* in the regulatory mechanisms of ACTH and cortisol release (6, 7). The parvocellular system of the paraventricular nucleus (PVN) containing CRH is probably the source of portal vasopressin. Indeed, vasopressin and CRH are present in the same secretory vesicles of the nerve terminals and vasopressin is known to potentiate CRH-induced ACTH secretion. Vasopressin release from the medial parvocellular PVN subdivision is thought to be independent of CRH release (9, 31). Oxytocin is less potent than vasopressin in enhancing ACTH release in rats (9). In humans, oxytocin appears to inhibit rather than to stimulate the release of ACTH (10).

Vasopressin has been reported to affect the release of some other pituitary hormones. Growth-hormone (GH) (32) and prolactin (33—35) release were shown to increase following i.c.v. vasopressin administration in rats; however, other studies (6) showed no GH release after using vasopressin in humans. It was then hypothesized (34, 35) that vasopressin may influence the prolactin

release directly or indirectly (i.e., through inhibition of dopamine release). On the contrary, other reports suggested that vasopressin inhibits prolactin release in rats (36, 37) but not in humans (6). Oxytocin is known to stimulate the suckling-induced prolactin release (38, 39).

The vasopressin and oxytocin in the regulation of thyrotropin hormone and thyroid hormones release

The role of vasopressin and oxytocin in the regulation of TSH release is still not clear. Incubation of bovine anterior pituitary slices in medium containing low concentrations of vasopressin stimulated the release of TSH (12). Lumpkin *et al.* (13) studied the effect of vasopressin on TSH release from rat adenohypophysis *in vitro* as well as *in vivo*: the rat anterior pituitary cells released more TSH when incubated with arginine vasopressin at doses ranging 10^{-9} to 10^{-5} M while 10^{-6} M oxytocin did not affect TSH release. *In vivo,* small i.c.v. doses of vasopressin (0.5 and 5.0 ng) suppressed the TSH secretion from 5 minutes after infusion on; this effect lasted at least for 60 minutes. In other experiments, intravenous injection of 0.06 IU/Kg of lysine vasopressin (LVP) had no effect on TRH-stimulated TSH release in humans (14). Immobilization stress was reported to increase the plasma vasopressin level but neither plasma TSH nor thyroid function were changed (40).

Present results (i.e., the increase of plasma TSH concentration after i.c.v. vasopressin in doses of 0.5 ng or 5.0 ng) are not consistent with experiments *in vivo* of Lumpkin (13). On the other hand, however, our results are quite compatible with the results *in vitro* of LaBella (12) as well as Lumpkin (13). We could noted, moreover, similar increase of FT_4 and FT_3 levels in plasma under vasopressin i.c.v. treatment. Exactly, complete agreement has been observed between plasma TSH level changes and FT_4 and FT_3 concentrations during vasopressin administration in both i.c.v. doses.

The progressive decrease of TSH, FT_4 as well as FT_3 plasma concentrations following i.c.v. treatment with 0.15 M NaCl (this study) deserves some comments. Similar effects on the TSH plasma level has been observed earlier following i.c.v. injections of normal saline (13) or normal rabbit serum (15). The phenomenon in question has not been commented by the authors mentioned (13, 15). It may be hypothesized, nevertheless, that the event may possibly be due to the temperature of the injected medium (being equal to room temperature, it was lower than the temperature of the rat brain).

TSH release from pituitary cells as induced by TRH in the rat was noted to be attenuated by oxytocin (41). Oxytocin, administered i.v., failed to change basal TSH and TRH-induced TSH secretion in humans (42). In other study, no effects of oxytocin on TSH secretion *in vitro* or *in vivo* in rat could be shown

(13, 36). Also, no effects following i.c.v. injection of antisera against oxytocin or vasopressin on TSH secretion have been observed in female rats (15).

In this study the effects of oxytocin injected i.c.v. in similar doses to vasopressin were not consistent. 0.5 ng i.c.v. of oxytocin was followed by the transient increase of TSH and FT_3 plasma levels but initial decrease of FT_4 plasma concentration with its increase at the end of the experiment. The i.c.v. oxytocin dose of 5.0 ng did not result the changes of TSH plasma values but increased the concentrations of FT_4 and FT_3 in blood plasma only at the beginning of the experiment. It is obvious that there was no parallel between the plasma levels of these hormones under treatment of oxytocin. The respective elucidation of this observation remains to the resolution.

It may be concluded that vasopressin modulate the function of the anterior pituitary — thyroid system. Vasopressin appears to stimulate the secretion of TSH and thyroid hormones. Oxytocin, however, does not show clear action in this process.

Acknowledgements. The authors wish to thank Professor Jan W. Guzek, Department of Pathophysiology, Medical University of Lodz, Poland, for kind discussion of the results here presented.

The authors appreciate the technical assistance of Mrs. Iwona Szklarska.

REFERENCES

1. Silverman AJ. Ultrastructural studies on the localization of neurohypophysial hormones and their carrier proteins. *J Histochem Cytochem* 1976; 24: 816—827.
2. Vandesande F, Diereckx K, de Mey J. The origin of the vasopressinergic and oxytocinergic fibers of the external region of the median eminence of the rat hypophysis. *Cell Tissue Res* 1977; 180: 443—452.
3. Gibbs DM. High concentrations of oxytocin in hypophysial portal plasma. *Endocrinology* 1984; 114: 1216—1218.
4. Lutz-Bucher B, Koch B. Characterization of specific receptors for vasopressin in the pituitary gland. *Biochem Biophys Res Commun* 1983; 115: 492—498.
5. Koch B, Lutz-Bucher B. Specific receptors for vasopressin in the pituitary gland: Evidence for downoregulation and desensitization to adrenocorticotropin-releasing factors. *Endocrinology* 1985; 16: 671—676.
6. Meller WH, Lewis DA, Gehris TL, Kathol RG. Human anterior pituitary response to exogenous arginine-vasopressin. *Acta Endocrinol (Copenh)* 1991; 125: 378—383.
7. Spinedi E, Negro-Vilar A. Arginine vasopressin and adrenocorticotropin release: correlation between binding characteristics and biological activity in anterior pituitary dispersed cells. *Endocrinology* 1983; 112: 2246—2251.
8. Antoni FA. Vasopressinergic control of pituitary adrenocorticotropin secretion comes of age. *Front Neuroendocrinol* 1993; 14: 76—122.
9. Gibbs DM. Immunoneutralization of oxytocin attenuates stress-induced corticotropin secretion in the rat. *Regul Pept* 1986; 12: 273—277.

10. Jenkins JS, Nussey SS. The role of oxytocin: present concepts. *Clin Endocrinol* 1991; 34: 515—525.
11. Richard P, Moos F, Freund-Mercier M-J. Central effects of oxytocin. *Physiol Rev* 1991; 71: 331—370.
12. LaBella FS. Release of thyrotropin *in vivo* and *in vitro* by synthetic neurohypophysial hormones. *Can J Physiol Pharmacol* 1964; 42: 75—83.
13. Lumpkin MD, Samson WK, McCann SM. Arginine vasopressin as a thyrotropin-releasing hormone. *Science* 1987; 235: 1070—1073.
14. Chiodera P, Gondi A. Marchesi C *et al.* Effect of lysine vasopressin on basal and TRH stimulated TSH and PRL release in normal men. *J Endocrinol Invest* 1988; 11: 497—500.
15. Franci CR, Anselmo-Franci JA, Kozlowski GP, McCann SM. Actions of endogenous vasopressin and oxytocin on anterior pituitary hormones secretion. *Neuroendocrinology* 1993; 57: 693—699.
16. Johansson O, Hökfelt T. Thyrotropin releasing hormone, somatostatin, and enkephalin: Distribution studies using immunohistochemical techniques. *J Histochem Cytochem* 1980; 28: 303—306.
17. Lechan RM, Jackson IMD. Immunohistochemical localization of thyrotropin-releasing hormone in the rat hypothalamus and pituitary. *Endocrinology* 1982; 111: 55—65.
18. Taylor T, Gyves P. Burgunder JM. Thyroid hormone regulation of TRH mRNA levels in rat paraventricular nucleus of the hypothalamus changes during ontogeny. *Neuroendocrinology* 1990; 52: 262—267.
19. Tsuruo Y, Ceccatelli S, Villar MJ *et al.* Coexistence of TRH with other neuroactive substances in the rat central nervous system. *J Chem Neuroanat* 1988; 1: 235—253.
20. Tsuruo Y, Hökfelt T, Visser TJ. Thyrotropin-releasing hormone (TRH)-immunoreactive cell groups in the rat central nervous system. *Exp Brain Res* 1987; 68: 213—217.
21. Horita A, Carino MA. Centrally administered TRH produces a vasopressor response in rabbits. *Proc West Pharmacol Soc* 1977; 20: 303—304.
22. Weitzman RE, Firemark HM, Glatz TH, Fisher DA. Thyrotropin-releasing hormone stimulates release of arginine vasopressin and oxytocin *in vivo*. *Endocrinology* 1979; 104: 904—907.
23. Ciosek J, Guzek JW. Influence of thyrotropin-releasing hormone (TRH) on vasopressin and oxytocin release: *in vitro* and *in vivo* studies. *Exp Clin Endocrinol* 1992; 100: 152—159.
24. Ciosek J, Guzek JW, Orłowska-Majdak M. Thyrotropin-releasing hormone (TRH) modulates vasopressin and oxytocin release from the hypothalamo-neurohypophysial system in dehydrated rats. *J Physiol Pharmacol* 1993; 44: 293—302.
25. Ciosek J, Stempniak B, Orłowska-Majdak M. Thyrotropin-releasing hormone (TRH) inhibits vasopressin release from hypothalamo-neurohypophysial system of rats drinking hypertonic saline. *Endocrine Regul* 1993; 27: 29—34.
26. Ciosek J, Orłowska-Majdak M. Thyrotropin-releasing hormone (TRH) inhibits the release of vasopressin but not that of oxytocin from the hypothalamo-neurohypophysial system in haemorrhaged rats. *Endocrine Regul* 1995; 29: 47—55.
27. Ciosek J, Stempniak B. Thyrotropin-releasing hormone (TRH) modifies oxytocin release from the hypothalamo-neurohypophysial system in salt-loaded rats. *J Physiol Pharmacol* 1995; 46: 169—177.
28. Ciosek J, Stempniak B. Thyrotropin-releasing hormone (TRH) inhibits vasopressin and oxytocin release from rat hypothalamo-neurohypophysiał explants *in vitro*. *Acta Neurobiol Exp* 1996; 56: 35—40.
29. Noble EP, Wurtman RJ, Axelrod J. A simple and rapid method for injecting ^{3}H-norepinephrine into the lateral ventricle of the rat brain. *Life Sci* 1967; 6: 281—291.

30. Tannahill LA, Dow RC, Fairhall KM, Robinson ICAF, Fink G. Comparison of adrenocorticotropin control in Brattleboro, Long-Evans, and Wistar rats. *Neuroendocrinology* 1988; 48: 650—657.
31. Sawchenko PE, Swanson LW, Vale W. Corticotropin releasing factor: coexpression within distinct subsets of oxytocin-, vasopressin-, and neurotensin-immunoreactive neurons in the hypothalamus of the adult male rat. *J Neurosci* 1984; 4: 1118—1129.
32. Heidingsfelder SA, Blackard WG. Adrenergic control mechanism for vasopressin-induced plasma growth hormone. *Metabolism* 1968; 17: 1019—1024.
33. Vaughan MK, Little JC, Johnson LY, Blask DE, Vaughan GM, Reiter RJ. Effects of melatonin and natural and synthetic analogues of arginine vasotocin and plasma prolactin levels in adult male rats. *Horm Res* 1978; 9: 236—246.
34. Blask DE, Vaughan MK, Champney TH *et al.* Opioid and dopamine involvement in prolactin release induced by arginine vasotocin and vasopressin in the male rat. *Neuroendocrinology* 1984; 38: 56—61.
35. Shin SH. Vasopressin has a direct effect on prolactin release in male rats. *Neuroendocrinology* 1985; 40: 55—58.
36. DePaolo LV, Bernardo PV, Carrillo AJ. Intraventricular administration of arginine vasopressin supresses prolactin release via a dopaminergic mechanism. *Peptides* 1986; 7: 541—544.
37. Mormede P, Vincent JD, Kerdelhue B. Vasopressin and oxytocin reduce plasma prolactin levels of conscious rats in basal and stress conditions. Study of the characteristics of the receptor involved. *Life Sci* 1986; 39: 1737—1743.
38. Lumpkin MD, Samson WK, McCann SM. Hypothalamic and pituitary sites of action of oxytocin to alter prolactin secretion in the rat. *Endocrinology* 1983; 112: 1711—1717.
39. Samson WK, Lumpkin MD, McCann SM. Evidence of a physiological role for oxytocin in the control of prolactin secretion. *Endocrinology* 1986; 119: 554—560.
40. Voropanova LS, Krasnowskaia IA, Sheiback TV, Sierska E, Polenov AL. Significance of hormonal feed back for hypothalamic nonapeptidergic center response to short-term immobilization stress in rats. *Biull Eksp Biol Med* 1993; 115: 128—130.
41. Frawley IS, Leong DA, Neill JD. Oxytocin attenuates TRH-induced TSH release from rat pituitary cells. *Neuroendocrinology* 1985; 40: 201—204.
42. Coiro V, Grundi V, Volpi R *et al.* Oxytocin enhances thyrotropin-releasing hormone-induced prolactin release in normal menstruating women. *Fertil Steril* 1987; 47: 565—569.

R e c e i v e d: December 19, 1996
A c c e p t e d: September 9, 1997

Author's address: J. Ciosek, Department of Physiology, Medical University of Lodz, Narutowicza 60, 90-136 Lodz, Poland