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THE EFFECTS OF SOMATOSTATINS ON THE PRL CELLS IN FEMALE RATS.

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Two biologically active molecular forms of somatostatin (SRIH), derived from a common 116 amino acids precursor have been characterized, the tetradecapeptide somatostatin-14 and the C-terminally extended form somatostatin-28 (Lewin and Romancer 1996). In the central nervous system SRIH acts as a neurotransmitter and/or neuromodulator and influences locomotor activity, cognitive functions and behavioral processes (Epelbaum 1986). Both peptides are also present in non-neuronal tissues such as the gastrointestinal tract and endocrine tissues including the pancreas, thyroid and adrenal gland (Reichlin 1983). Somatostatin inhibits the secretion of several non-pituitary hormones such as insulin, glucagon, gastrin, secretin and aldosterone (Epelbaum 1986; Milošević 1999). It is well known that SRIH inhibits release of growth hormone (GH) from somatotropes via separate receptors in the plasma membrane (Reichlin 1983). Hypothalamic SRIH also inhibits the secretion of thyrotropin-stimulating hormone (TSH) and prolactin (PRL) from the anterior pituitary (Epelbaum *et al.* 1994). The effects of SRIH on PRL cells has not been systematically studied. There is the evidence that at pituitary level, SRIH inhibits prolactin secretion, but at the hypothalamic level it may increase prolactin secretion possibly by reducing dopamine release (Gillies1997). This study was designed to evaluate the effects of intracerebroventricular (i.c.v.) administration of low doses of SRIH-14 and SRIH-28 on the morphology and secretory activity of PRL cells in pituitary glands of female rats.

The study was performed on adult female Wistar rats (210-230*g*). The rats were implanted with a headset later used for i.c.v. injections. A minimum recovery time of 5 days was permitted before the onset of experiments. The animals were divided into three experimental groups each consisting of five animals. The first and the second group consisted of rats given (i.c.v.) every second day three 1-μg doses of SRIH-14 or SRIH-28 dissolved in 5 μL saline. The third group was the control treated in the same manner, except that the animals received i.c.v. 5 μL of saline. All animals were sacrificed by decapitation during deep anaesthesia 5 days after the last injection. Pituitary glands were excised, fixed in Bouin's solution and embedded in paraffin. Serial 5μm thick tissue sections were deparaffinized. Pituitary PRL cells were localized by the peroxidase-antiperoxidase-complex (PAP) method of Sternberger *et al.* (1970). Measurements were performed on the widest portion of the pituitary gland and immunocytochemically-labelled PRL cells were analyzed by the M_{42} test system after Weibel (1979). For the calculations of the cell and nuclear volumes the formula of Weibel (1979) was used. Serum concentrations of PRL in control and experimental rats were measured by the Delfia method. Biochemical and morphometric data obtained from each group were averaged, and the standard deviation of the mean was calculated. A one-way analysis of variance (ANOVA), followed by the multiple range test of Duncan was used for statistical comparisons between the groups. A probability value of 5% or less was considered statistically significant.

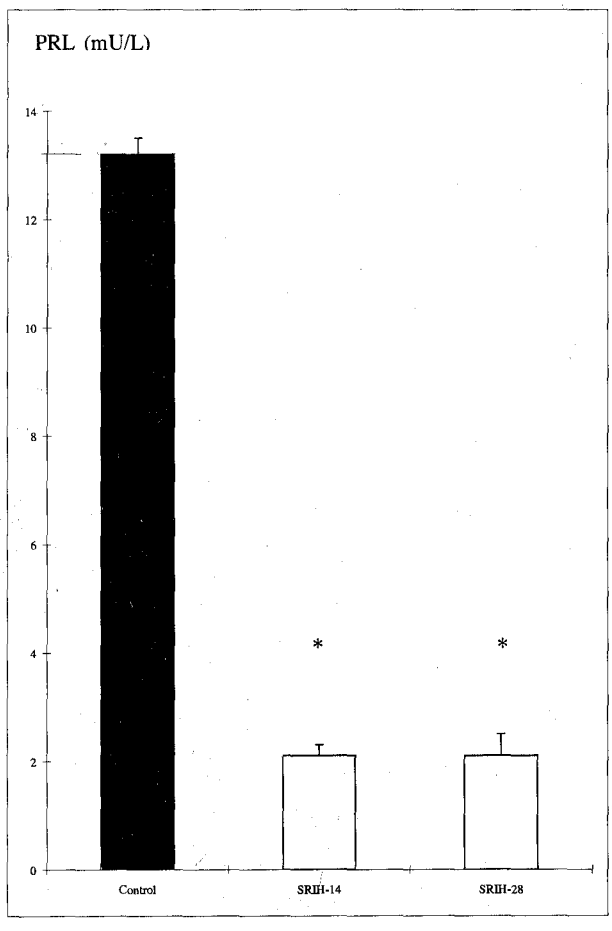
Immunocytochemically labeled PRL cells in the control pituitaries were polygonal, elongated in shape, with a spherical centrally located nucleus. PRL cells were usually surrounded by large oval gonadotropic cells. These cells were sparse in the anterior-ventral portion of the gland. In i.c.v. SRIH-treated female rats PRL cells were smaller, irregularly shaped, with more intensely black secretory granules. All morphometric parameters were decreased ($p<0.05$) in comparison with the control (Table 1). Serum PRL level in both SRIH-14- and SRIH-28-treated females was significantly decreased ($p<0.05$) by 85%, as compared to the control (Fig. 1).

Table 1. Morphometric parameters of the pituitary PRL cells after intracerebroventricular administration of SRIH-14 or SRIH-28 to female rats.

Experimental group	Volume of the PRL cells (mm^3)	Volume of the PRL muclei (mm^3)	Volume density of the PRL cells (%)
Control	770 ± 24.0	148 ± 13.4	30 ± 1.3
SRIF-14	6.30 ± 0.1*	102 ± 10.4*	17 ± 0.7*
	(-18%)	(-31%)	(-43%)
SRIF-28	655 ± 2.8	115 ± 5.6*	19 ± 1.4*
	(-15%)	(-22%)	(-37%)

(means ± SD; n = 5); *p<0.05, in comparison with the control.

These changes were similar to those obtained in male rats treated in the same manner with SRIH-14 or SRIH-28 (Milošević *et al.* 1998). PRL cells are acidophils as GH cells and PRL could be an ancestral molecule for GH (Pantić 1990). A number of reports describe transformation of GH cells into PRL cells as well as somatomammotropes and mammosomatotropes (Takahashi 1992).



In summary, intermittent exposure of female rats to i.c.v. SRIH-14 or SRIH-28 reduces serum PRL concentracions with the corresponding changes in morphology of PRL cells that secrete these hormones.

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Fig. 1. Serum concentration of PRL after intracerebroventricular administration of SRIH-14 of SRIH-28 to adult female rats. Data are expressed as the means ± SD. (n=5), * $p<0.05$ in comparison with the control.