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DISSERTATION SUMMARY

Effects of different galanin compounds and fragments on vasopressin and oxytocin secretion in rats

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Following the discovery of galanin (GAL) in the porcine intestine (Tatemoto et al. 1983), many data have been reported as concerns its physiological effects. These results suggest that the 29 amino acid-containing GAL plays a significant role as a peptide modulator in the regulation of the function of the hypothalamo-neurohypophyseal system. Aims: The effects of rat, porcine, human GAL and the 1-16 N-terminal and 16-30 C-terminal fragments of human GAL on vasopressin (VP) and oxytocin (OT) secretion were studied in rats. The question was investigated of whether the GAL receptor antagonist galantid (M15) was able to prevent the VP and OT level changes induced by GAL. Finally, the direct effects of GAL on VP and OT production were examined in isolated neurohypophyseal (NH) tissue cultures (an in vitro study).

Following intravenous (i.v.) or intracerebroventricular (i.c.v.) administration of GAL, the plasma VP and OT levels were determined by radioimmunoassay (RIA). Basal plasma VP and OT concentration elevation were induced by osmotic (2.5% NaCl solution) or non-osmotic (histamine - HA) stimuli, or lactation. To make the isolated NH tissue cultures, we used an enzymatic dissociation technique. The VP and OT contents of the supernatants of 14-day cultures were determined by RIA.

GAL administered i.v. (9.6 µg/kg) did not influence the basal or the stimulated VP and OT excretion. After the i.c.v. injection of GAL (0.32 µg/kg), the basal VP and OT levels did not change. The plasma VP and OT concentration enhancements induced by intraperitoneal NaCl administration, or lactation were prevented by prior treatment with i.c.v. GAL. The HA-induced elevations in plasma VP and OT levels were significantly moderated by i.c.v. GAL administration. During lactation, the higher OT level was decreased after GAL administration.

There was no essential difference in the VP and OT release effects of rat, porcine and human GALs. The two investigated human GAL fragments had different effects: the human GAL 1-16 fragment proved active as concerns VP and OT regulation, whereas the human GAL 16-30 fragment proved ineffective.

The GAL receptor antagonist M15, administered i.c.v. before the GAL injection, prevented all of the VP- and OT-responsive effects of GAL.

After the administration of increasing doses (10^{-13} – 10^{-6} M) of GAL, linear decreases were detected in the VP and OT contents of the supernatant medium in the isolated NH tissue culture.

The present results demonstrate the important role of GAL in the regulation of VP and OT secretion following different forms of stimulation: an osmotic response, HA administration or lactation. Our findings lead us to conclude that the 1-16 N-terminal GAL fragment contains the biologically active centre of the GAL molecule (Molnar et al. 2005). The results of experiments with isolated NH tissue cultures indicate that the GAL-ergic system can directly influence the hormone-producing activity of the pituicytes.

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