Dopaminergic regulation of avian prolactin gene transcription

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Abstract

It is well documented that prolactin (PRL) release and PRL gene expression in birds are controlled by the tonic stimulation of hypothalamic vasoactive intestinal peptide (VIP). However, there is good evidence that dopamine (DA) exerts both stimulatory (at the hypothalamic level) and inhibitory (at the pituitary level) effects on PRL secretion. The interactions between VIP and DA in the regulation of PRL gene transcription are not known. This study was designed to examine the effects of a D_2 DA receptor agonist (D_2AG; R(−)-propylnorapomorphine HCl) on basal and VIP-stimulated PRL gene transcription rate, PRL mRNA steady-state levels, PRL mRNA stability and PRL release from cultured turkey anterior pituitary cells. The D_2AG (10^{-10} M) completely inhibited the stimulatory effect of VIP (10^{-7} M) upon nascent PRL mRNA as determined utilizing a nuclear run-on transcription assay. To examine further the effect of the D_2AG on PRL mRNA post-transcriptional events, anterior pituitary cells were treated with different concentrations of D_2AG (10^{-12}–10^{-4} M). Semi-quantitative RT-PCR and RIA were performed to determine the levels of PRL mRNA and PRL content in the medium respectively. The results show that D_2AG inhibited VIP-stimulated PRL mRNA steady-state levels as well as basal and VIP-stimulated PRL release, effects which were diminished by the D_2 DA receptor antagonist, S(−)-eticlopride HCl (10^{-10} M). Actinomycin D (5 μg/ml), an inhibitor of mRNA synthesis, was used to assess the effect of D_2AG on PRL mRNA stability in response to VIP. The stimulatory effect of VIP on PRL mRNA stability was completely negated by the D_2AG (from a half-life of 53·0±2·3 h in VIP-treated cells to 25·5±1·6 h in D_2AG+VIP-treated cells, $P \leq 0{\cdot}05$). These results support the hypothesis that VIP and DA play a major role in the regulation of PRL gene expression in avian species, at both the transcriptional and post-transcriptional levels. In addition, these findings suggest that the DAergic system inhibits PRL release and synthesis by antagonizing VIP at the pituitary level via D_2 DA receptors.

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