



Maturation of Prolactin Secretion in Females: Experimental Models Help to Reveal its Probable Importance in the Intergenerational Mode

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Abstract

It is suggested that more attention should be attracted to maturation of prolactin secretion in females during postnatal development, especially after perinatal exposure to stress or glucocorticoids in excess. For this aim experimental models on rats and pituitary cell cultures can be efficiently used, outlining the possibility of studies on intergenerational transfer of disease risk by changing the adaptation to lactation through altered prolactin function.

Keywords: Experimental Models; Ontogeny; Prolactin

Introduction

In the last Editorial in this journal (in press) we began some discussion on a role of prolactin in women's health. However, due to principal importance of this hormone in the maintenance of lactation, we decided to pay more attention to maturation of prolactin secretion in postnatal ontogeny. In fact, since our PhD thesis, we have dedicated a significant amount of our research efforts for studying this question in experimental models on rats and especially, in primary cell cultures. Here are the main results.

Maturation of prolactin secretion in postnatal ontogeny

At first, we need to explain that prolactin is the principal hormone secreted in primary cultures of adenohypophyseal cells in adult rats [1]. However, in cultures of neonatal rats not prolactin, but growth hormone (GH) is the main hormonal protein produced [2]. Nevertheless, during postnatal development the situation is reversed: gradually prolactin becomes the principal component of hormonal protein secretion, especially in females [3,4] (see also Figure 1-3).

In spite of this huge ontogenetic difference, neonatal lactotrophs, i.e. prolactin-producing cells are already capable to respond to hypothalamic hormones (thyrotropin-releasing hormone, somatostatin and dopamine) by altered secretion in a mode, quite similar to that of adult animals [4].

DOHaD concept and phylopathogenic model

Earlier we have already proposed the importance of DOHaD concept for providing much better health and well-being to future human generations, as referred to anemias [5]. In relation to this concept, during the last 12 y we are elaborating two theoretical models, of the onto- and phylopathogeny [6].

Ontopathogenic model is already rather well established, explaining how the etiopathogenic mechanisms are developed during the whole ontogeny including pre- and postnatal stages, through intermediate age categories and till the senescence [7], whereas phylopathogenic model tries to understand how predisposition to

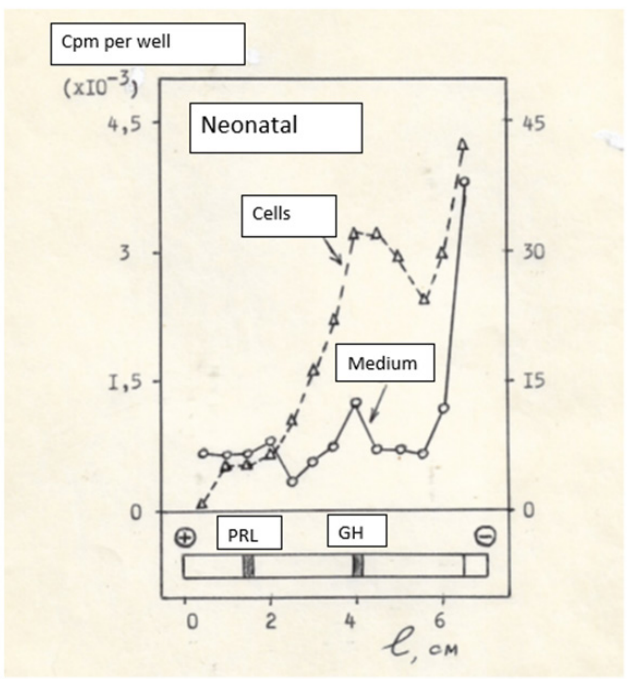


Figure 1: Representative run of disc-electrophoresis in polyacrylamide gel for proteins prelabelled with ^{14}C -L-leucine in cellular homogenate and incubation medium of neonatal rat pituitary cells in primary culture.

Left and right ordinate axes are for medium and cells respectively.

Abbreviations here and on Figure 2 and 3: Cpm – counts per min, l – length along cylindric gel (in cm), circled signs of – and + – negative and positive electrodes respectively, PRL – prolactin, GH – growth hormone.

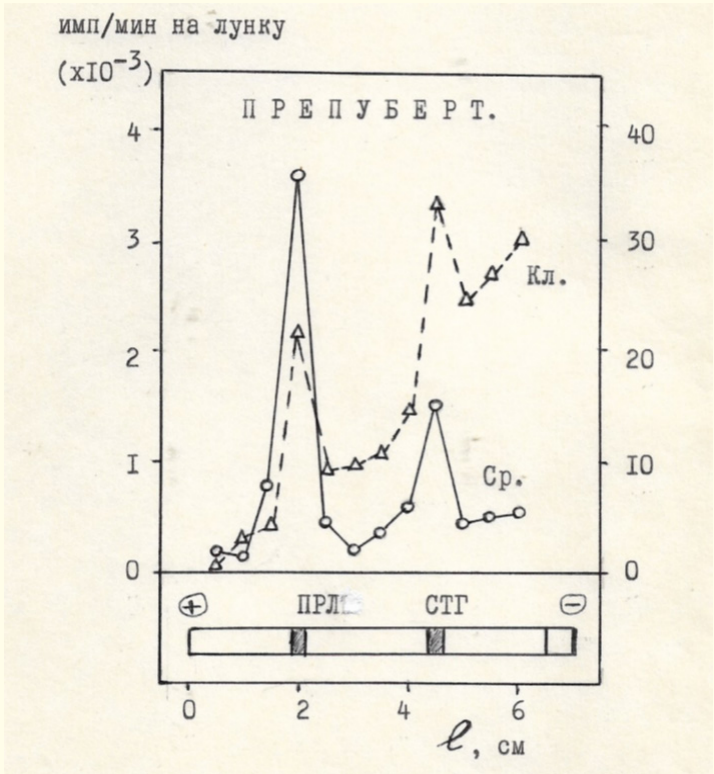


Figure 2: The same as on Figure 1, but for prepubertal animals.

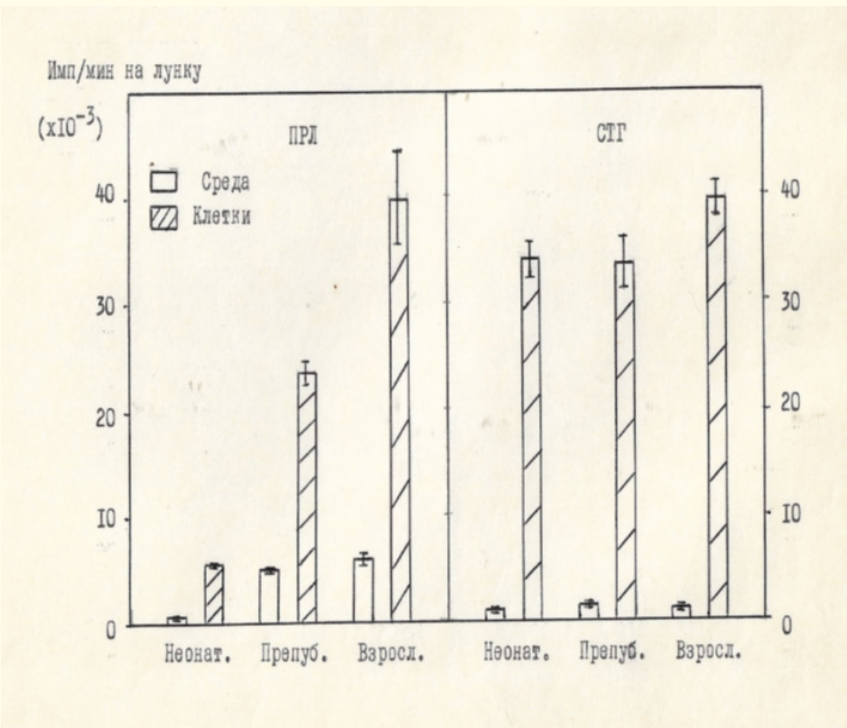


Figure 3: Statistical treatment for PRL and GH secretion in pituitary cell cultures of neonatal, prepubertal and adult female rats (the differences for PRL are highly significant, as compared to neonatal animals).

various diseases can be transferred in the inter-, multi- and trans-generational mode. In fact, ontopathogenic model is a particular case of phylopathogenic one, since the health situation in pregnant mother can directly influence the offspring in at least the intergenerational mode (generations $F_0 \rightarrow F_1$).

Here is the main reason, why the phylopathogenic model deserves much higher attention than before. In fact, only just recently the first suggestions appeared on the role of glucocorticoids and stress for intergenerational transfer of disease risk. One of the main hypotheses tries to explain this phenomenon by altering the adaptation of female body to higher gestational demands [8]. But what about lactation?

Roles of glucocorticoids and stress in regulation of prolactin function

Although this topic was poorly investigated till the present time, nevertheless some scarce data suggest inhibitory action of stress

and glucocorticoids on prolactin secretion [9]. It is interesting that in contrast, glucocorticoids stimulate GH secretion, at least in vitro, although they inhibit DNA and total protein synthesis in cultured hypophyseal cells [10,11].

Why is this evidence so important? The research group of Julia Buckingham in UK was able to show that perinatal glucocorticoids can interfere with lactotropic function in offspring [12]. It means that future mothers exposed to glucocorticoids or stress can have lower degree of adaptation not only to pregnancy, but also to lactation.

On the other hand, long-term investigations of research group of Michael Meaney in Canada have already demonstrated that the type of behavior of lactating mother may influence their offspring also [13].

All these data suggest that phylopathogenic model has very interesting perspectives of elaboration already in the near future. By the way, it appears that Dino Giussani in Cambridge University was the first to discover the evidence supporting phylopathogenic model in human population [14]. In fact, the comparison of birthweights in subpopulations of Bolivia living or not in high altitude clearly show that long-term consequences of chronic hypoxia due to high altitude may influence the transfer of cardiometabolic risk, according to DOHaD concept, i.e. quite similar to effects of anemias.

Final comments

In conclusion, the studies on the role of glucocorticoids and stress in prolactin function should be continued. The experimental approach elaborated by us earlier allows to investigate in comparative mode the regulation of prolactin secretion by adenohypophyseal cells explanted from animals exposed to glucocorticoids in early life (in experimental scheme $\text{in vivo} \rightarrow \text{in vitro}$). Moreover, not only the inter- ($F_0 \rightarrow F_1$), but also multi- or transgenerational mode (at least $F_0 \rightarrow F_2$ or even $F_0 \rightarrow F_3$) can be applied, in order to amplify the evidence obtained.

The obtaining these data cannot be pursued in humans, since bioethics strictly prohibit invasive procedures in pregnant or lactating women and in children. In addition, only laboratory mammals with short duration of gestation and the whole lifespan (rats, mice and hamsters) can be efficiently used, in order to make all this experimentation really possible and the results obtained reliable.

In any case, it is our conviction that women's health and future generations should be benefited also by experimental preclinical modeling.

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