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Review Article

Pineal and Coccygeal Glands with Some Functions Poorly Defined: Perspectives for Near Future

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Abstract

In this article we try to call for more interest to poorly studied aspects of pineal gland, as well as to coccygeal gland – complete mystery in modern endocrinology. Special attention is devoted to our own studies on primary monolayer cell cultures of these glands, together with long-term investigations of several Russian researchers on pineal peptides and melatonin.

Key words: pinealocytes; melatonin; coccygeal gland; peptides

Introduction

During the eighties of the last century there occured our fruitful contacts with Yaroslav A. Sokolov, a physician who worked earlier in the Laboratory of Biological Research of Hormonal Compounds of the Institute of Experimental Endocrinology in Moscow, Russia. He had communicated to us about a theoretical study [1] performed together with his father A.A. Sokolov, a professor of exact sciences. This study described a scheme of localization of endocrine glands along the vertical axis of human (and animal) body (without legs) in the following order (from top to bottom):

Pineal gland (epiphysis) → Pituitary gland (hypophysis) → Thyroid / parathyroid glands → Pancreas (islets of Langerhans) → Adrenals → Gonads (testes / ovaries) → Coccygeal gland

If the majority of these endocrine glands and their hormonal products are already well known (except thymus), the pineal and especially coccygeal gland remain poorly investigated till the present moment. Therefore, we decided to reunite some scarce data including our own observations, in the attempt to attract some attention to this theme.

Poorly Studied Aspects of Pineal Gland

Of course, some topics related to pineal gland are already well-known recalling melatonin in the first place. However, melatonin is produced not only by pinealocytes, but also by neuroendocrine cells of gastro-intestinal tract [2]. Moreover, melatonin is already well-known bioregulator in plants. Finally, due to its physico-chemical properties, melatonin is an excelent antioxidant. Although the role of pineal gland and melatonin in the maintenance of circadian and seasonal biorhythms is also well established, nevertheless the question remains: what are the other functions of this organ and by which bioregulators (besides melatonin) are they executed?

At first, we need to remember some old speculations, beginning with postulate of Rene Descartes about pineal gland as a place where human soul is situated [3]. Moreover, Brazilian spiritism considers this organ as antenna necessary for spiritual communication [4]. Curiously enough, Russian researcher Alexey M. Olovnikov, the person who was the first to suggest the existence of telomeres, has launched an hypothesis about pineal gland as lunasensor, necessary for counting infradian rhythms [5].

During the eighties of the last century, working in the same laboratory and institute as Yaroslav A. Sokolov did, especially on adenohypophyseal cell cultures, we have tested finally an idea about the possibility of isolation and cultivation of pituitary and pineal cells in parallel, since both are located respectively upon and under the brain (epiphysis / hypophysis cerebri) and therefore, can be explanted from the same animal head.

However, at that time we had in our hands only the analytical methods for evaluation of principal adenohypophyseal hormones: growth hormone and prolactin by means of electrophoresis in polyacrylamide gel (after prelabelling with 14C-L-leucine) and radioimmunological assays. Therefore, whe have used pineal gland cultures in two ways:

1) by obtaining conditioned medium of pinealocytes and applying it to pituitary cell culture, in order to evaluate its influence on prolactin secretion;
2) by realizing the hybrid pituitary / pineal cultures as some sort of “cellular Frankenstein”.

In the first case, we were successful to show that conditioned medium of pinealocytes diluted 5-fold was able to inhibit prolactin secretion in two modes: stimulated prolactin release in short-term incubation, as well as basal prolactin secretion in long-term experiment [6]. Although the prolactin-inhibitory pineal bioregulator(s) remained unidentified, we

argued that conditioned pinealocytes medium may be a better source for their isolation, than the whole pineal glands, since the former does not contain contaminants of intracelular proteins.

In the second case of hybrid pineal / pituitary cultures the data remained unpublished, although the secretory product of pinealocytes in pure (not hybrid) culture appeared to possess weak immunoreactivity of human corticotropin, according to dilution test in parallel with standard preparation.

We have shown also higher sensitivity of cultured pituitary cells of neonatal rats to melatonin, according to inhibition of DNA synthesis, as compared to cells of adult animals [7]. Moreover, we reviewed bibliographical data on antistress activity of melatonin in early ontogeny and in aging [8, 9].

Finally, during the last 50 years a group of Russian researchers (V.K. Khavinson, V.N. Anisimov aand their colleagues) has elaborated and applied in clinical medicine several preparations isolated from or identified in pineal gland (epithalamin, epitalon) [10, 11]. These preparations were already used as geroprotectors or agents for treating some age-related disorders. Twenty years ago, in 2005 we have visited both these researchers in St. Petersburg (see Figure.1). It is interesting also that V.N. Anisimov has dedicated a lot of time for studies of melatonin and pineal preparations as anticancer agents.

In conclusion, modern methods of isolation and characterization of various bioregulators should be applied to pineal gland in near future. In addition, old suggestions about the transport of pineal hormones to biological fluid of cerebral ventricles through tanycytes, the cells of ependynal origin should be evaluated by means of modern imaging technologies, thus trying to explain finally the strategic location of pineal gland in close contact with nervous tissue.

Figure 1: Our meeting with Vladimir N. Anisimov (on the right) at the Institute of Oncology, St. Petersburg, Russia, in 2005.

Mysterious Functions of Coccygeal Gland

First of all, we should warn the interested readers that this gland appears to be a distinct feature of only some species of deers. However, we must remember that human fetus has a tail in some stage of organogenesis, although this remnant is completely dissolved in later stages. What about the coccygeal gland of deers, in the eighties of the last century we were able to obtain primary culture of its cells in glass Carrel flask, observing huge lipid-like droplets of putative secretory product floating on the surface of culture medium (unpublished results). Again, primary cell culture could be an excellent source of unidentified bioregulators from coccygeal gland, without the necessity for hunting the deers, in order to obtain this precious tissue material.

Also at the same period of time a book of Russian scientist I.I.Brekhman was published in Brazil. This book contained a short note about a zone close to coccygeal gland in small-size deers, with putative gonadotropic activity, thus explaining its proximity to the gonads [13]. Many years later we have found some data about this mysterious gland in quite unusual way. The matter is that near the city of Santa Maria in the center of the state of Rio Grande do Sul in Brazil there exists so called 4th Colony of Italian immigrants, what perhaps was the reason for Italian scientist and manager Antonio Meneghetti to organize a new faculty that now takes his name and is located in beautiful place called Recanto Maestro (https://www2.faculdadeam.edu.br/).

Looking for details about the activities of Antonio Meneghetti in Italy and Brazil, we have found unexpectedly that this outstanding researcher has published once an article about coccygeal zone [14], probably because of his great interest to biomedical aspects related to psychosomatic medicine. However, unfortunately the nature of bioative substances probably secreted by this gland remains a complete mystery till the present time.

Final Remarks

Famous proverb affirms that new things are in fact old things that were already forgotten. Recently we have published in this journal a short commentary about putative metabolic inhibitor in anterior pituitary gland that remains unidentified till the present moment [15], in spite of all the progress in biochemistry and molecular biology during the last decades. Perhaps, the time has come to remember finally about these forgotten data. In conclusion, modern endocrinology has a lot of rather obscure aspects that need much closer attention of present and future generations of research workers all over the world, independently of sometimes remote places where they perform numerous investigations. Fortunately, stable and rapid Internet communication, together with available and

foregoing tools of Artificial Intelligence, make possible, at least, theoretical and bibliographic studies, in order to accelerate more substantial experimental endeavors.

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This article is dedicated to the memory of Vladimir N. Anisimov and Vladimir K. Khavinson, outstanding Russian scientists that applied a lot of their research efforts for studies of melatonin and pineal peptides.

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