Endocrinology & Diabetes: Open Access Journal

Iris Publishers

Short Communication

Adrenals and Pituitary as Endocrine Glands Responsible for Stress Reactions: An Update

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Received Date: December 16, 2022

Published Date: December 23, 2022

Abstract

This article is devoted to short description of some poorly studied aspects of adrenals and pituitary, as referred to their participation in responses to stress. In addition, putative schemes for cytodifferones of these endocrine glands are briefly discussed.

Keywords: Adrenal cortex; Anterior pituitary; Cytoarchitectonics; Stress

Abbreviations: ACTH: Adrenocorticotropic Hormone; CRF / CRH: Corticotropin-Releasing Factor / Hormone; FSH: Follicle-Stimulating Hormone; GC: Glucocorticoids; GH: Growth Hormone; HPA: Hypothalamo-Pituitary-Adrenal (axis); LH: Luteinizing Hormone; MSHa: Melanocyte-Stimulating Hormone Type Alpha; PRL: Prolactin; TSH: Thyroid-Stimulating Hormone

Introduction

It may appear at first that this topic has been already studied in a comprehensive mode. The goal of this mini review is to show that, as a matter of fact, this theme is quite far from clear yet, in spite of all the progress in hormonal physiology and pharmacology, biochemistry and molecular biology. In order to do this, we shall try to find out the lacunes in our present knowledge, especially as referred to stress reactions.

What is the physiological significance of pituitary and adrenal glands? The pituitary is considered as a chief endocrine gland regulating the functional activities of many other glands, as well as growth and lactation. On the other hand, since the seminal works of Thomas Addison in 19th century, it is clear that adrenals are essential for survival of humans and animals.

It is interesting also that blood perfusion of adrenal glands is higher than in kidneys, and it increases even further under the influence of adrenocorticotropic hormone (ACTH) [1]. Moreover, in the case of intrauterine growth restriction during the 3rd trimester of pregnancy, the growth of adrenals, together with brain and heart, is affected much less, than the rest of fetal body, what designates a phenomenon of asymmetric growth restriction [2,3].

Another peculiarity of adrenals is the high content of ascorbic acid, a well-known antioxidant, probably necessary for counteracting radical oxygen species generated during hydroxylation of corticosteroid precursors [4]. And of course, the vital importance of adrenocortical hormones becomes evident in the cases of adrenal insufficiency, for example after abrupt cessation of pharmacotherapy with synthetic glucocorticoids (GC) that provoke adrenal atrophy.

Adrenal Cortex and Medulla

In adult animals and humans there exist important interactions between these two principal parts of adrenal glands. In fact, it appears that some kind of analogue of hypothalamo-pituitary-

adrenal (HPA) axis takes place in the adrenal medulla [5-7], however its relationship with hypothalamic corticotropin-releasing factor or hormone (CRF / CRH) and pituitary ACTH is poorly understood. On the other hand, GC appears to stimulate the functional activities of adrenal medulla.

Moreover, the cytokinetics in adrenal cortex is not clear yet. The cambial layer of stem or progenitor cells is located probably in zona glomerularis [8], and there is tissue streaming from this layer to zona fasciculata and reticularis. Earlier we offered a general hypothetical scheme of adrenal cytodifferone, according to which there is a sequential commitment of adrenocortical cells in the following order of hormone production [9].

Precursor or stem cells -> mineralo- or GC -> ouabain -> weak androgens

This sequence recapitulates probably anterior pituitary cytodifferone (see later in this article).

What is the importance of these ideas for regulation of stress reactions? It is assumed that the main products of adrenal medulla, the catecholamines (noradrenaline and adrenaline, or norepinephrine and epinephrine) characterize, first of all, the acute stress, whereas GC, cortisol in humans and corticosterone in rats, are more related to chronic type of stress [10]. Nevertheless, their interconnections, especially in circadian, ultradian and infradian biorhythms were not studied yet.

Pituitary Gland

This gland is composed of anterior pituitary (or adenohypophysis), as well as intermediate lobe and neurohypophysis. The last two parts produce respectively melanocyte-stimulating hormone type alpha (MSHa) and a couple of neuropeptides, arginine vasopressin and oxytocin. The anterior pituitary is a principal part of the gland, secreting several so-called tropic (or trophic) hormones. Earlier we offered the following hypothetical sequence of commitment of their production in adenohypophyseal cytodifferone [9].

Progenitor or stem cells -> ACTH -> TSH -> LH/FSH -> GH/PRL -> PRL/GH

If to compare this scheme with that of the adrenal cytodifferone, it becomes clear that ACTH corresponds to mineralo- and GC, TSH – to ouabain and LH/FSH – to weak androgens. Moreover, we suggest that these sequences of commitment are related to dramatic evolutionary changes of environment for early vertebrates, from salty water of oceans and seas to saltless water of rivers and lakes (ACTH & mineralo-/GC), then to the coastal land (TSH & ouabain) and finally to the earth regions, far away from the coast (LH/FSH & weak androgens). In addition, we suggest that these stages correspond to ontogenetic transitions revealed by us during analysis of somatic growth plots for humans and partially for rats [11] in such a way: ACTH & mineralo-/GC - to infantile transition, TSH & ouabain - to juvenile transition and LH/FSH & weak androgens - to pubertal transition.

In this regard, GH and PRL appear to be the pituitary hormones, dependent on previous stages (ACTH & mineralo-/GC, TSH & ouabain and LH/FSH & weak androgens), considering also that TSH and gonadotropins regulate thyroid and sex steroid hormones respectively.

What about the involvement of pituitary hormones in stress regulation? At present it is well known that ACTH is produced in anterior pituitary by proteolytic processing of proopiomelanocortin (POMC) in corticotrophs. However, in anterior pituitary, besides ACTH, also beta-endorphin and beta-lipotropin are produced, whereas in the intermediate lobe MSHa is produced. How this processing is regulated, in order to differentiate the production of various hormonal POMC derivatives, is not clear yet. Complicating this topic even further, the receptors for ACTH and MSHa are called melanocortin receptors, and in order to provide the specificity of ACTH binding and action, a special mechanism is employed (see discussion in [12]). Moreover, the roles of beta-endorphin, beta-lipotropin and MSHa in stress regulation are not well studied yet.

Even for ACTH there are certain doubts in this respect. Really, there exist many situations where secretion of ACTH and GC is dissociated from each other [13]. Moreover, in adrenocortical cultures ACTH does not stimulate cell proliferation, but in contrast, this tropic hormone causes its inhibition [7, 8], what contradicts to the classical scheme of HPA axis and even to the proper name of ACTH or corticotropin, i.e., the hormone tropic (or trophic) for adrenal cortex.

What for other pituitary hormones, it is already clear that stress reactions involve GH and PRL release. Moreover, PRL stimulates adrenal cortex, whereas GC appears to inhibit PRL secretion [4,14]. However, what is the significance of GH and PRL involvement in regulation of HPA axis functions, is not clear yet.

Final Comments

As can be seen, at present we are far from comprehensive understanding of HPA axis functions, including those of the adrenals and pituitary gland, especially as referred to their chronobiological interactions. However, translational perspectives are great for hormones, but not for behavior, because of huge differences in central nervous system between humans and laboratory animals (like rats and mice) frequently used as experimental models. Therefore, the participation of psychologists performing psychometric tests on human volunteers is indispensable for our advancement in the concepts and ideas about stress and its mechanisms.

This is especially relevant, if to remember that in particular the brain is the principal organ involved in stress reactions. However, due to the greater complexity of this topic, we pretend to dedicate for it our separate publication.

Acknowledgement

This work has not received financial support from any source.

Conflict of interest

The authors affirm that conflict of interest does not exist.

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