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Review

Stress hormones, sleep deprivation and cognition in older adults

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ABSTRACT

Cognition can be deteriorated in older persons because of several potential mechanisms including the hormonal changes occurring with age. Stress events cause modification in hormonal balance with acute and chronic changes such as increase in cortisol and thyroid hormones, and simultaneous alterations in dehydroepiandrosterone sulphate, testosterone and insulin like growth factor-1 levels. The ability to cope with stress and regain previous healthy status, also called resiliency, is particularly impaired in older persons Thus, stressful conditions and hormonal dysregulation might concur to the onset of cognitive impairment in this population.

In this review we address the relationship between stress hormones and cognitive function in older persons focusing on the role of one of the main stress factors, such as sleep deprivation (SD).

We extracted and cross-checked data from 2000 to 2013 March and selected 112 full-text articles assessed for eligibility. In particular we considered 68 studies regarding the contribution of hormonal pathway to cognition in older adults, and 44 regarding hormones and SD both in rats and humans.

We investigated how the activation of a stress-pattern response, like the one evoked from SD, can influence cognitive development and worsen cognitive status in the elderly.

We will show the limited number of studies targeting the effects of SD and the consequent changes in stress hormones on cognitive function in this age group.

We conclude that the current literature is not strong enough to give definitive answers on the role of stress hormonal pathway to the development of cognitive impairment in older individuals.

Contents

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1. Introduction

1.1. Hormonal changes with aging and after stressful conditions

Aging is marked by subtle incremental changes in all biological systems, including endocrine ensembles.

In older people generally there is a prevalence of catabolic hormones such as thyroid hormones, thyroxine (T4) and triiodothyronine (T3), and cortisol. These hormones known as "stress hormones", are involved in the genesis of stress-related conditions implying the activation of adrenergic axis.

The autonomic sympathetic-adrenal system and the hypothalamic–pituitary–adrenal (HPA) axis are considered to be the main neuroendocrine systems involved in the integrated stress response. The activation of the body's stress systems and the release of stress hormones allows us to adapt and survive in a continuously changing and challenging environment. These stress hormones not only support metabolic processes and physical activity under acute stress but also affect brain function, cognition and mood [1].

A challenge provokes the activation of several mechanisms related to stress response, with the increase of epinephrine and norepinephrine, cortisol, and thyroid hormones. The age-related changes in stress hormones are paralleled by the profound decline of anabolic hormones dehydroepiandrosterone and its sulfate derivative (DHEA and DHEAS), testosterone, estradiol, growth hormone (GH) and insulin growth factor-1 (IGF-1) concentrations resulting in a net increase of catabolic/anabolic ratio.

After a challenge there is a recovery phase with a return to a basal condition of the genesis of a new level of balance. The age-related changes in the pattern of HPA response to challenge influence the individual's resiliency in the on-going homeostatic regulatory processes of the body [2]. Aging has been more often associated with an hyper-activation of HPA axis in response to a stimulus. Interestingly, the ability of HPA axis to recover from a challenge (resiliency), is more affected than the rate of the initial response or the magnitude of the response [3,4]. The changes of the HPA function occurring with age show a heterogeneous pattern, with some individuals maintaining a pattern similar to those of younger subjects and others experiencing substantial changes with aging. Despite this heterogeneity, the response of HPA axis to stress with age becomes less resilient and less sensitive to the negative feed-back signals of glucocorticoids (GC). As consequence, the altered HPA axis as part of multiple hormonal dysregulation occurring with age, may exert an important role of the development of cognitive impairment in the elderly. If age seems to be the most relevant pathogenic factor for the altered HPA sensitivity toward the steroid inhibition, the occurrence of neurodegenerative cognitive impairment could play an additional role leading to a vicious cycle "HPA axis hyper activation-cognitive impairment".

The mechanism by which aging influences pituitary function is complex. Comorbidities and adaptations that accompany aging strongly modify the pituitary secretion. In particular, the effects of age on endocrine axes depend on hormone type, inhibitor or stimulus tested, concomitant morbidities, such as obesity, diabetes mellitus, reduced nutritional status, medication use, underlying stress, body composition and gender [5].

Aging-related changes in the HPA axis are more prominent in women than in men, and in patients with Alzheimer disease or major depression.

When homeostatic mechanisms maintaining neuronal function are overwhelmed, the reactive processes must be set in motion.

Moreover, there are changes of the adrenocortical steroidogenetic pattern occurring during aging, with a relative constancy or even a trend toward an increase of cortisol secretion and a progressive age-related decline of the androgen secretion. Both cortisol and DHEA affect metabolism, and the balance between these two hormones has been considered as a marker of catabolic/anabolic status, relating to frailty [6]. The adrenocortical secretory pattern undergoes qualitative and quantitative changes with aging. In particular, beside a relatively steady level of cortisol secretion, there is a trend toward higher plasma levels during evening- and night-time [7].

DHEA and DHEAS production dramatically decrease with aging, and during the eighth decade is only 10–20% of the maximal value usually recorded at 30 years. The imbalance between glucocorticoid and androgen secretions may be caused by the age-related selective impairment of the "zona reticularis" of the adrenal cortex, the sole source of DHEA and DHEAS (Fig. 1).

In fact, the complex vascular supply of the adrenal gland, characterized by communications between the cortex and medulla with reciprocal functional influences, is the anatomical basis for the peculiar susceptibility of the zona reticularis to microhemorrhagic events and vascular necrotic damage, which in turn is responsible for the age-related decline in androgen secretion [8].

As consequence, an imbalance between GC and androgens occurs in the elderly. It is well known that cortisol and DHEAS have opposite activities both at peripheral and central levels.

Aging is accompanied by a decrease in pulsatile GH secretion, IGF-1 levels and an increase in IGFBP-1 and IGFBP-3.