
Related Hormonal Deficiencies and Their Association with Neurodegenerative Diseases

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Abstract: In recent years, in general worldwide aspects, birth rates are falling, and life expectancy is rising, resulting in an increasing rate of population aging. The occurrence of this moderate decline in aging is normal, however there are dementia syndromes, in which this decline is marked. Thus, the research will demonstrate a study involving hormonal deficiencies in general, and, as a main research objective, those involving age and also involving the association with neurodegenerative diseases. In this perspective, the bibliographical research was chosen, and, in order to accomplish it, a dialectical evaluation of the positions of competent theorists will be carried out in relation to the subjects discussed, and the data will be evaluated through interpretation, analysis, and comparisons about the subjects worked on. Cognitive decline in the elderly has become a growing concern due to the pace of population aging and its potential deleterious effect on the quality of life of individuals. Identifying people who are more likely to suffer from cognitive decline makes it possible to establish interventions to prevent delay or even reverse cognitive changes.

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1. Introduction

Diseases are understood to be those that directly attack the nervous system, that is, they affect the neurons of the human brain, the basic unit of the nervous system. Neurons do not normally reproduce or replace themselves, so when they are damaged or die, they cannot be replaced. Parkinson's disease, Alzheimer's disease and Huntington's disease are some examples of neurodegenerative diseases.

According to Baddeley, Anderson and Eysenck [1], the human brain undergoes important changes in healthy aging. There is a shrinkage in brain areas that affect memory, learning, planning and other complex activities; regions such as the prefrontal cortex and the hippocampus. Therefore, there is a modest decline in cognitive ability as we age.

The Elderly Statute was created with the main objective of ensuring the well-being of the elderly, preserving their mental and physical health, so that it defines the elderly as people who are sixty years of age or older [2]. In recent years, in general terms, birth rates have been falling worldwide, and life expectancy has been rising, which has resulted in an increasing rate of population aging. Old age is not a split in relation to previous life, but is, in fact, a continuation of adolescence, youth, and maturity that may have been lived in different ways.

The occurrence of this moderate decline in aging is normal, but there are dementia syndromes in which this decline is accentuated. Thus, the research will demonstrate a study involving hormonal deficiencies in general and, as the main research objective, those involving age and, also, involving the association with neurodegenerative diseases. In addition, the research raises the existing problem regarding the need to relate hormonal problems linked to diseases linked to the central nervous system with the age of patients.

Furthermore, given the introduction presented, the main objective of this work is to elaborate a context involving the main types of neurodegenerative diseases, according to an age aspect, that is, according to the most studied

and increasingly developing diseases; academic study of age -related hormonal deficiencies ; and practical and current discussion of age - related neurodegenerative diseases – their direct and indirect relationships. In this perspective, we opted for bibliographical research, and, to carry it out, a dialectical evaluation of the positions of competent theorists in relation to the subjects discussed will be performed, with the data being evaluated through interpretation, analysis and comparisons about the subjects worked on.

2. Development

Before we delve into the main theme of this research, age-related hormonal deficiencies and their association with neurodegenerative diseases, it is necessary to approach both themes separately, to better understand their history, as well as their development, specifically , throughout human life , considering that numerous studies indicate that moderate decline with aging is normal , however , certain syndromes called dementia can lead to a sharp decline and , consequently, the appearance of neurodegenerative diseases or even the worsening of existing ones .

Thus, this chapter will aim to initially demonstrate age-related hormonal deficiencies through the study of the human body and its substances responsible for the creation of hormones, as well as their maintenance. Next, the second part will address neurodegenerative diseases , in order to highlight the need for study, given the information on disabilities resulting from age - human beings are born with millions of neurons , however , over the course of their lives, they are lost , which do not have the capacity to recreate themselves , consequently, their lack leads to dementia diseases , which are popularly found in older individuals .

Diagnostic and Statistical Manual of Mental Disorders (DSM-5, APA, 2014), the term dementia is still used as a synonym for neurocognitive disorders because it is commonly used by physicians and patients. These disorders refer to conditions that affect younger people, such as impairment due to HIV infection or impairment secondary to traumatic injury, but it is also the nosological category to refer to degenerative disorders, which typically affect older adults.

2.1 Age -Related Hormonal Deficiencies

The human body has several substances responsible for regulating the normal functioning of organic activities. Among them, hormones stand out, which are produced in the endocrine glands. Endocrine glands are organs that secrete substances into the blood, known as hormones. Since they are not produced correctly, it is natural for the body to be more susceptible to diseases, in the presence of hormonal disorders.

Endocrinology is the area of medicine that aims to recognize and treat problems with these hormones, helping to restore the body's balance. The field of activity of the endocrinologist is extremely vast, since hormones regulate practically all organic functions and, therefore, hormonal changes can cause several diseases, involving the body as a whole.

The endocrine system is made up of a group of glands and organs that regulate and control various functions of the body through the production and secretion of hormones. Hormones are chemical substances that affect the activity of another part of the body. In essence, hormones act as messengers that control and coordinate activities throughout the body.

The levels of most hormones decrease with aging, but the levels of some hormones remain at the same levels as in younger adults, and some even increase. Even when hormone levels do not decrease, endocrine function normally declines with age because hormone receptors become less sensitive. Some hormones that decrease in levels include estrogen (in women), testosterone (in men), growth hormone, and melatonin.

In women, a decline in estrogen levels leads to menopause. In men, a gradual decrease in testosterone levels usually occurs. Low levels of growth hormone can cause a decrease in muscle mass and endurance. A decrease in melatonin levels may be a major cause of the loss of normal sleep-wake cycles (circadian rhythms) as a person ages.

Li and Singh [3] state that Alzheimer's disease affects three times more women than men. These authors also state that women are more severely affected by it. In this case, lose their verbal advantage due to the decline in estrogen after menopause and, therefore, men begin to have an advantage in tasks and tests of episodic, verbal and

visuospatial memory. Zhang et al. [4] showed that sex hormones have effects on AD, with women being more vulnerable to the disease and having a more marked AP compared to men.

Estrogen and progesterone are the predominant sex steroid hormones in women and are present in lower concentrations in men. Estrogen is produced in women in three forms, as estrone (E1), estradiol (E2) and estriol (E3). They are produced mainly by the ovaries in women, but can also be synthesized by the brain, as occurs when contraceptives are used. During the menstrual cycle, there are two peaks of E2 secretion, the first just before ovulation and the other during the luteal phase. In adult men, estradiol modulates sexual behavior and organizes the brain for sexual behavior, being involved in the modulation of libido, erectile function, and spermatogenesis. In addition, this hormone also affects the amount of serotonin receptors in the brain, which are involved in the modulation of mood and cognition. Sex hormones appear in many studies related to brain development, mood, and cognition. Estrogen, especially E2, has neurotrophic effects, improves cerebral blood flow, and promotes synaptic plasticity and myelination. Thus, it can be stated that endogenous female sex hormones have neuroprotective and anti-aging properties, therefore hormone deprivation during menopause could explain women's vulnerability to cognitive decline. After menopause, E2 circulates in higher concentrations in the male body than in the female body) [5,6].

In this direction, the study by Rasgon et al. [7] showed that the reproductive period and the age of menopause were inversely proportional to the cognitive decline in women. In other words, the longer the reproductive period in years (difference between the age of menarche and menopause) and the more advanced the age in years of menopause, the better the cognitive performance of women. Fox, Berzuini and Knapp [8], presented a series of studies that expose the inhibitory role of estrogen on the formation of beta -amyloid protein, responsible for the formation of plaques in the brain. There is also evidence that estrogen inhibits the hyperphosphorylation of tau protein and reduces inflammation in the brain, among other neuroprotective functions.

During normal aging (in the absence of neurodegenerative disease) hippocampal neurons are largely preserved with little or no decrease in the number of dentate granule neurons and CA3 pyramidal neurons, and only a modest loss of CA1 neurons. However, the ability of neurons to communicate with each other may be compromised during aging as a result of decreased numbers of dendritic spines and synapses [9].

Evaluation of spatial learning ability in rats of different ages demonstrated an adverse effect of aging on hippocampal-dependent learning and memory, which is associated with reductions in long -term potentiation (LTP) of synaptic transmission at CA1 hippocampal synapses. However, results from other studies suggest that age-related impairment of hippocampal-mediated cognitive function can occur without synapse loss [10].

Neural stem cells located in the subgranular region of the dentate gyrus of the hippocampus are capable of proliferating and differentiating into functional neurons that integrate into the hippocampal circuitry. Recent findings suggest that hippocampal neurogenesis is diminished during aging, an effect counteracted by energy restriction through diet and exercise, manipulations that attenuate age-related hippocampal dysfunction [11].

Electrophysiological methods have been used to assess neuronal excitability, neurotransmitter sensitivity, and synaptic plasticity in the aged hippocampus. CA1 neurons in hippocampal slices from aged rats exhibit prolonged calcium - dependent afterhyperpolarizations compared with CA1 neurons from young rats, which may result from increased calcium influx through voltage - gated calcium channels [12].

An age-related deficiency of LTP at hippocampal CA1 synapses has been consistently reported, and similar LTP deficits may also occur at synapses of dentate granule and CA3 neurons. LTD induction is increased at CA1 synapses in old rats compared with young rats, a change that would be expected to impair learning and memory capacity. It has been suggested that disturbed calcium release from the endoplasmic reticulum plays a role in the increased LTD that occurs in hippocampal neurons during aging [13]. Collectively, the data suggest that reduced excitability and LTP and increased LTD occur in hippocampal neurons during aging and may contribute to age-related hippocampal dysfunction.

Patients with Alzheimer's disease exhibit profound disruption of their circadian rhythms and a loss of pulsatility of neuroendocrine systems. Given that the hippocampus is a major site of neurodegenerative pathology in Alzheimer's disease, it is reasonable to consider that damage to this brain region contributes to the disturbed regulation of neuroendocrine systems in this disease. Examples of hormones that are normally released in a pulsatile fashion but are released in a dysregulated fashion in Alzheimer's disease include cortisol [14], vasopressin [15], and melatonin [16]. When taken together with the data from animal studies described below, the correlation

of hippocampal pathology with dysregulated neuroendocrine pulsatility in Alzheimer's disease is consistent with a prominent role for the hippocampus in the control of neuroendocrine rhythms.

The classical trisynaptic circuit within the hippocampus has been studied extensively with respect to synaptic connectivity and function. However, the structure and function of extrahippocampal projections are less well understood. The hippocampal subiculum is the primary source of afferent input to the hypothalamus. There appears to be some subfield specificity for subicular afferents to the hypothalamus, because the vast majority of neurons identified by tracing studies are located in the ventral subiculum. Axonal projections from this region join the corticohypothalamic tract, which passes through the PVN and SCN before terminating in the dorsomedial and mammillary nuclei of the hypothalamus. Ventral subicular fibers form synapses in these regions, allowing them to influence neuroendocrine function. Within the PVN, the anatomical pattern of ventral subicular afferents is nearly identical to the distribution of SCN afferents [17]. This anatomical similarity supports the idea that hippocampal information about prior experiences converges with SCN information about the diurnal state to modulate hormonal pulsatility.

The flow of information between the hippocampus and the SCN is essentially unidirectional, because the vast majority of monosynaptic afferents from the SCN terminate in the hypothalamus. However, the SCN projects to the PVN, which sends reciprocal inputs back to the ventral subiculum of the hippocampus. This anatomical data indicates that the hippocampus receives input from the hypothalamic PVN and sends information to the PVN and SCN. However, no studies to date have evaluated possible changes in the size and strength of hippocampal - hypothalamic connections in aged animals.

2.2 Neurodegenerative Diseases of Age

Neurodegenerative diseases are very debilitating conditions, still without a cure, that affect people of all ages and result from the progressive degeneration and/or death of neurons – the cells responsible for the functions of the nervous system. This degradation can affect body movement – ataxias – and brain function, leading to dementia. These diseases are one of the most important medical and socioeconomic problems of today, and the causes of their appearance are still unknown. As time passes, some neurons are lost and die, and our body is only capable of producing a very small number of new neurons. This inability to produce new nervous system cells is a natural process related to aging.

Therefore, it is necessary to address so-called dementia diseases, that is, those linked to the decrease or loss of cognitive capacity due to age – it is important to mention that senility is not always linked to the appearance of these, although, in the majority, pathological diseases are linked to the elderly.

Dementias are divided according to age into senile dementia and presenile dementia. Presenile dementia begins before the age of 65 and senile dementia occurs after this age. The age of onset of dementia is extremely important, as an early onset may be evidence that there is a strong genetic component and, therefore, blood relatives will be more likely to also develop the same disorder.

Dementia is not a specific disease; it is a general term used to designate a series of symptoms that are linked to the progressive impoverishment and impairment of all psychics, cognitive and affective processes, which occur due to changes in the nervous tissue of the brain. To a large extent, this impoverishment occurs in the organization of feeling and thought. The multiple losses of cognitive and functional abilities involve, for example, memory loss, changes in executive functions, personality changes, the presence of diffuse changes in brain tissue and associated psychiatric symptoms, such as paranoia and depression, may arise [18].

The DSM-5 (APA, 2014) lists the following subtypes of neurocognitive disorders: Alzheimer's disease (AD), frontotemporal lobar degeneration, Lewy body disease, vascular disease, traumatic brain injury, substance / medication use, HIV infection, prion disease, Parkinson 's disease, and Huntington 's disease. AD is the main neurodegenerative disease associated with aging. It is characterized by mitochondrial dysfunction, oxidative stress, synaptic failure, and cognitive decline.

3. Discussion

The United Nations, through Resolution 39/125, during the First United Nations World Assembly on Population Ageing (1982), was responsible for producing an International Plan of Action in Vienna. Subsequently, in 1991, the General Assembly adopted the United Nations Principles for Older Persons, enumerating 18 rights of older persons, all related to independence, participation, care, self-realization and dignity of older people.

The following year, the International Conference on Ageing met to follow up on the Plan of Action by adopting a Declaration on Ageing. Following the recommendation of the Conference, the UN General Assembly declared 1999 the International Year of Older Persons. Thus, the International Day of Older Persons is celebrated on 1 October each year.

Consequently, action on behalf of aging continued in 2002 with the Second World Assembly on Aging in Madrid, which had as one of its objectives the development of an international policy on aging in the 21st century. A Political Declaration and the Madrid International Plan of Action on Aging were adopted, which called for changes in attitudes, policies and practices at all levels in order to respond to aging in the 21st century.

Old age is not a split in relation to previous life, but is, in fact, a continuation of adolescence, youth and maturity that may have been lived in different ways. Historical circumstances, which he relates to both private and public life, play a very important role in the determinants of old age.

Although it is less precise, the chronological criterion is one of the most widely used to establish an elderly person. In Brazil, in October 2003, Law No. 10,741 was published, which establishes the Elderly Statute and other provisions. Thus, initially, in its preliminary provisions, people aged 60 or over are given priority and full protection, according to their needs.

Art. 1 The Elderly Statute is hereby established, intended to regulate the rights guaranteed to people aged 60 (sixty) years or over.

Art. 2. The elderly enjoy all fundamental rights inherent to the human person, without prejudice to the full protection provided for in this Law, ensuring them, by law or other means, all opportunities and facilities to preserve their physical and mental health and their moral, intellectual, spiritual and social improvement, under conditions of freedom and dignity.

Art. 3 It is the obligation of the family, the community, society and the Public Authorities to ensure that the elderly, with absolute priority, have the right to life, health, food, education, education, culture, sport, leisure, work, citizenship, freedom, dignity, respect and family and community life.

As for old age, its concept needs to be viewed as the last phase of the human aging process, since old age is not a process like aging, but rather a state that characterizes the condition of the elderly human being. Furthermore, the elderly are the reflection of the entire history of living in the place, so their rights, primarily to safety and quality of life, must be guaranteed as an instrument of comprehensive protection.

Furthermore, in summary, the Elderly Statute [2] was created with the main objective of ensuring the well-being of the elderly, preserving their mental and physical health. Art. 1 defines that the elderly consist of people who are sixty years of age or older. In developed countries, birth rates are falling, and life expectancy is rising, which results in an increasing rate of population aging. According to the Brazilian age pyramid for the Brazilian population from 2012 to 2018, published by IBGE (2018), there was a decrease at the base of the pyramid indicating a smaller number in the younger age groups and at the same time an increase in the percentages at the top of the pyramid.

Neurodegenerative diseases are progressive degenerative processes that become more serious as the years go by. Patients may, for example, have motor problems ending up immobile or in a wheelchair; have breathing difficulties that can cause death; have cognitive problems or problems related to gradual memory loss, eventually affecting the memory of everything learned throughout life. These diseases have a major impact on the professional, social and family life of patients, and can lead to a total inability to carry out any type of daily activity. For this reason, the caregivers and family members who accompany these patients on a daily basis also end up being invisible victims of the disease, making it easy to imagine the strong negative impact that a disease of this type has on the family unit.

One of the main problems that occurs in patients with neurodegenerative diseases is the fact that they are detected late, when the patient has already lost more than 50% of their neurons. In other words, by the time the patient goes to the doctor and the diagnosis is known, the disease is already very advanced, and treatment options are of limited effectiveness. In recent years, scientists have gained greater knowledge about neurodegenerative diseases, minimizing the side effects of treatments and improving the type of medications used to control symptoms. However, the causes of these diseases are still unknown and, therefore, none of these diseases have a cure and some are fatal. It is only known that 1 to 10 % are hereditary.

Cognitive decline in old age has become a growing concern due to the pace of increasing population aging and its potential deleterious effect on individuals' quality of life. Identifying people most likely to suffer from cognitive decline allows interventions to be established to prevent it; delay or even reverse cognitive changes. It is essential that society supports scientific research in this area, to accelerate the discovery of the causes and mechanisms of neurodegenerative diseases and to develop preventive treatments that are more appropriate to the symptoms of each disease. Solidarity says a lot about each one of us, and the discovery of a cure and more effective treatments depends on research but also on the help of all of us.

4. Final Considerations

The Elderly Statute was created with the main objective of ensuring the well-being of the elderly, preserving their mental and physical health, so that it defines that the elderly consist of people who are sixty years of age or older. In recent years, in general terms worldwide, birth rates have been falling, and life expectancy has been rising, which results in an increasing rate of population aging.

Thus, it is observed that with the increase in the elderly population, there is a need to address diseases involving age, since it is known that many appear after a certain age, with preventive monitoring being important, according to hormonal exams, which are clearly related, albeit indirectly, with neurodegenerative diseases.

proved to be important insofar as age-related hormonal deficiencies may be directly or indirectly linked to neurodegenerative diseases, given the conclusion that over the course of human life, there is an evident moderate decline in mental faculties which, in general terms, does not change human life, that is, although they exist, they do not cause considerable damage. However, certain syndromes called dementia can lead to a sharp and consequent decline, the appearance of neurodegenerative diseases or even the worsening of existing ones.

Furthermore, it is concluded that the direct association of some neurodegenerative diseases with the elderly population and with the gradual aging of the world population suggests that they will have an enormous social impact during the 21st century. The degradation of neurons can cause various types of neurodegenerative diseases that affect brain function, leading to dementia. In general terms, dementia consists of the progressive or chronic decline in cognitive function, which affects memory, thought, behavior, language, calculation ability, learning and emotion, and should never be associated with a normal aging process.

The decline in old age has become a growing concern due to the increasing pace of population aging and its potential deleterious effect on individuals' quality of life. Identifying individuals most likely to suffer from cognitive decline allows interventions to be established to prevent, slow down, or even reverse cognitive changes.

Author Statements:

- **Ethical approval:** The conducted research is not related to either human or animal use.
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