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ALZHEIMER: A FORGOTTEN DISEASE

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Abstract: OBJECTIVE: As we age, some changes occur in different areas of our cognition and behavior, and these changes occur in a temporal order. People over 65 often complain of difficulties with memory and other cognitive abilities compared to their own performance in previous years. Thinking about the prevalence of AD and other dementias that affect cognition, this complaint is understandable and requires careful attention. The objective of this work was to describe the main etiologies of Alzheimer's and its respective treatment. RESULT AND DISCUSSION: Sudden changes in cognition can predict the onset of AD within an approximate period of seven years. In longitudinal research carried out by Sliwinski et al. (1996) apud (Kaszniak AW 2001), where patients with pre-clinical symptoms of AD were included, significant effects of age on cognition were found. Therefore, many changes are not common to normal aging, but are the result of changes that precede AD. In research comparing groups of patients with frontotemporal dementia (FTD), mild AD and normal elderly people, it was found that the AD group presented more severe episodic memory deficits and visual-spatial impairments. As for executive functions, they showed milder impairments at the beginning of the disease than those observed at the beginning of FTD. However, some executive dysfunctions are present at the beginning of the disease, and perhaps these patients who present these difficulties are part of a subgroup of AD, with severe frontal neuropathology. The FTD group demonstrated severe impairment of executive functions and episodic recall memory with greater preservation of recognition memory in the early stages (Perry RJ, Hodges JR, 1999). CONCLUSION: The numerous studies reviewed above demonstrate that executive functions act directly on the global

cognitive functioning and activities of daily living of the elderly. Knowing that changes in these functions can be observed in normal elderly people and are generally observed in patients with AD, it is important to carry out a differential diagnosis and refer them to appropriate treatments. Finally, it is important that future research investigates in a systematic and controlled manner the heterogeneity of cognitive deficits observed in AD, as in the case of patients with predominantly executive function deficits.

Keywords: Alzheimer's; Etiology; Aging.

INTRODUCTION

Alzheimer's disease (AD), characterized by the German neuropathologist Alois Alzheimer in 1907, is a progressive and irreversible neurodegenerative disease with an insidious onset, which causes memory loss and various cognitive disorders. In general, late-onset AD, with an incidence around 60 years of age, occurs sporadically, while early-onset AD, with an incidence around 40 years of age, shows familial recurrence. Late-onset AD and early-onset AD are the same and indistinguishable clinical and nosological unit (HARMAN D, 1996).

As life expectancy becomes higher, especially in developed countries, an increase in the prevalence of AD has been observed. This condition represents around 50% of dementia cases in the USA and Great Britain and is estimated to be the fourth leading cause of death among elderly people in these countries. (KACHATURIAN ZS. 1975)

From a neuropathological point of view, diffuse cortical atrophy, the presence of a large number of senile plaques and neurofibilar tangles, granulo-vacuolar degeneration and neuronal loss are observed in the brain of individuals with AD. There is also an accumulation of b-amyloid protein in senile plaques and tau microtubulin in neurofibrillary tangles. It is believed that the concentration of senile plaques is correlated with the degree of dementia in those affected. Disorders of acetylcholine and acetyltransferase transmission frequently occur in affected individuals (KATZMAN R. 1986) The changes observed in the brains of those affected can also be found in healthy elderly people, but not jointly and to such an intensity. The course of the disease varies between 5 and 10 years and the reduction in life expectancy is around 50% (HARMAN D, 1996). The objective of this work was to describe the main etiologies of Alzheimer's and its respective treatment.

METHOD

This is a literature review, of a narrative type, which aims to describe Alzheimer's disease, from etiology to treatment, from a theoretical point of view, through materials that have already been published on the topic in question, through analysis and interpretation of literature. The inclusion criteria were: articles in Portuguese and English; published between 2014 and 2023 and which addressed the themes proposed for this research, review-type studies made available in full. The exclusion criteria were: duplicate articles, available in abstract form, which did not directly address the proposal studied and which did not meet the other inclusion criteria.

The review was carried out from July to September 2023, through searches in the databases Virtual Health Library (VHL), Latin American and Caribbean Literature in Health Sciences (LILACS), *National Institutes of Health's Library of Medicine* (PubMed) and *Scientific Electronic Library Online* (SciELO). The following descriptors were used: "Alzheimer", "Etiology", "Aging", in order to find articles relevant to the subject covered. After the selection criteria, 6 articles

remained that were subjected to thorough reading for data collection. The results were presented in a descriptive way, divided into thematic categories addressing: describing the subtitles or points that were mentioned in the discussion.

RESULT AND DISCUSSION

The genetic factor is currently considered preponderant in the etiopathogenesis of AD among several related factors. In addition to the genetic component, toxicity to infectious agents, aluminum, oxygen free radicals, neurotoxic amino acids and the occurrence of damage to microtubules and associated proteins were identified as etiological agents (YING W.1996; MALAMUD DN. 1972) It also acts through direct damage to the genetic material, leading to a somatic mutation in the tissues. (SMITH MAC, 1996)

As we age, some changes occur in different areas of our cognition and behavior, and these changes occur in a temporal order. For example, it is expected that changes will occur first in visual-spatial and visual-constructive tasks than in verbal tasks. People over 65 often complain of difficulties with memory and other cognitive abilities compared to their own performance in previous years. Thinking about the prevalence of AD and other dementias that affect cognition, this complaint is understandable and requires careful attention.

Furthermore, deficits in cognitive functions in the elderly can cause, depending on their degree, loss of independence, increased mortality rate and reduced quality of life. Therefore, it is not surprising that the scientific effort that has currently been invested in better understanding the cognitive decline of healthy elderly people (Wilson RS, Bennett DA, Swartzendruber, A, 1997)

Studies in elderly people indicate that there are progressive changes with typical characteristics of aging. One of the main complaints observed is related to the difficulty in evoking recent events known as Benign Senescent Forgetfulness. There are studies that suggest that these changes would be at the limit of initial cases of AD and Depression. Neuropsychological theories were developed based on this evidence in order to explain memory changes in healthy elderly people. In this article, we will talk specifically about the Frontal Cortex Theory, responsible for executive functions (Morris R. 1997).

Sudden changes in cognition can predict the onset of AD within approximately seven years. In longitudinal research carried out by Sliwinski et al. (1996) apud (Kaszniak AW 2001), where patients with pre-clinical symptoms of AD were included, significant effects of age on cognition were found. Therefore, many changes are not common to normal aging, but are the result of changes that precede AD.

Cognitive changes in normal aging present qualitative and quantitative differences in relation to those observed in AD. In the Brown-Peterson test, normal elderly people show no changes while patients with AD show impairment (Puckett JM, Lawson WM. 1989)

In AD, brain atrophy does not occur predominantly in the frontal region, but in the temporal and parietal lobe. The same occurs with neurofibrillary tangles, which appear in the frontal cortex as the disease progresses. However, there must be a subgroup of AD with particular neuropathological severity in the frontal region (Johnson JK. Et al 1999). Although memory and language have received the most attention in neuropsychological research, executive functions also appear to be particularly vulnerable since the onset of AD (Kaszniak AW 2001). There is evidence that some patients have a greater degree of deficits in executive functions than others.

According to Perry and Hodges Perry RJ,

(Hodges JR 1999), after an initial amnestic stage in patients with AD, divided attention is generally the next deficit observed in this disease, even before the impairment of language and visual-spatial functions. This data confirms difficulties in activities of daily living presented by patients since the beginning of AD, such as following conversations involving more than one person, or in places with a lot of noise. These difficulties are due to deficits in executive function, such as divided attention or working memory. This difficulty is even worse when the social situation is complex or new. Even patients who are still in the initial phase of the disease may show signs of these difficulties (Goldberg E. 2001).

At the beginning of AD, the three subtypes of attentional functions (selective, divided and amplitude) are not affected in the same way. While divided attention and aspects of selective attention are particularly vulnerable, attentional breadth or attention span/ immediate memory is relatively preserved (Perry RJ, Hodges JR 1999). Although attention is part of executive functions, tests that measure attention are different from those that assess executive functions, as the former include precise information at the beginning of the application, such as what to do and when to finish. Executive functions, on the other hand, require more problem solving, which requires planning, monitoring, strategy, and also attention (Brennan M, Welsh MC, Fisher CB. 1997)

Volition, as we said previously, is one of the components of executive functions. This is altered in AD, where apathy and passivity are seen in more than 70% of patients with mild AD and in 90% of severe cases (Gilley DWç. Et al 10991). In relation to these data, neuropsychological and neuroimaging studies revealed an association of these behavioral deficits with dysfunction of the frontal system (Kaszniak AW. 2001). It was also observed that 25% of patients with AD presented disinhibition and inappropriate social behaviors (Kaszniak AW. 2001). Studies were carried out to verify the correlation between agitated behavior and disinhibition using neuropsychological tests. They reported deficits in 4 tests that assess executive functions in agitated and disinhibited patients, such as verbal fluency, Stroop, WCST and Trail B (Kaszniak AW. 2001).

In the Stroop and Trail B tests, impairments were observed in mental flexibility, and also in divided attention. While in the WCST, patients with AD often present a higher incidence of perseverative errors. In the Clock Drawing test, conceptual errors, perseveration and errors regarding the space limit were verified Rouleau I, et al 1992). Other losses found in patients with AD refer to intrusion errors, a difficulty that is not seen in healthy elderly people, as well as impairment of visual-constructive skills (Dalla Barba G, Wong C, 1995)

More recently, several studies have investigated the capacity for awareness or insight in AD patients about their cognitive deficits. This difficulty in becoming aware of one's own difficulties and limitations is called anosognosia. In research comparing groups of patients with frontotemporal dementia (FTD), mild AD and normal elderly people, it was found that the AD group presented more severe episodic memory deficits and visual-spatial impairments. As for executive functions, they showed milder impairments at the beginning of the disease than those observed at the beginning of FTD. However, some executive dysfunctions are present at the beginning of the disease, and perhaps these patients who present these difficulties are part of a subgroup of AD, with severe frontal neuropathology. The FTD group demonstrated severe impairment of executive functions and episodic recall memory with

greater preservation of recognition memory in the early stages (Perry RJ, Hodges JR, 1999).

CONCLUSION

The numerous studies reviewed above demonstrate that executive functions act directly on the global cognitive functioning and activities of daily living in the elderly. Knowing that changes in these functions can be observed in normal elderly people and are generally observed in patients with AD, it is important to carry out a differential diagnosis and refer them to appropriate treatments.

Regarding cognition, normal aging and AD, the literature converges in several aspects. Among them, with advancing age, most elderly people experience a decline in their cognitive functions, mainly associated with memory capacity. The cognitive decline observed in AD is especially evident in relation to anterograde episodic declarative memory, working memory, and processing speed. Finally, it is important that future research investigates in a systematic and controlled manner the heterogeneity of cognitive deficits observed in AD, as in the case of patients with predominantly executive function deficits.

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