



Amyloid Plaques and Alzheimer's Disease



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Abstract

In cognitive aging, the process of brain atrophy is accelerated over the years and is characterized mainly by the deposition of beta-amyloid peptide (A β). In this review using the DeCS descriptors "placa amilóide and Doença de Alzheimer" and their English version, which resulted in the selection of 7 studies. Amyloid plaques and intraneural neurofibrillary tangles involved in the alterations that occur in neuritic processes and glial cells are the most important features of Alzheimer's disease. According to the amyloid cascade hypothesis, the accumulation of A β is the main cause of degeneration and cognitive decline.

Keywords : Placas amilóides; Doença de Alzheimer; Amyloid Plaque; Alzheimer's Disease

Abbreviations : AD: Alzheimer's Disease; APP: Amyloid Precursor Protein

Introduction

Aging is a natural process that affects all individuals and that causes various changes in the organism [1]. In cognitive aging, the process of brain atrophy is accelerated over the years and is characterized by dilatation of sulci and ventricles, loss of neurons, presence of amyloid plaques and neurofibrillar tangles, deposits of beta-amyloid protein, and granulovacuolar degeneration. These changes appear early in medial temporal lobe regions and spread throughout the neocortex [2].

The neuronal loss, synaptic degeneration, senile plaques and neurofibrillar tangles found in neurological diseases represent the main pathological findings of Alzheimer's disease (AD). The last two alterations are the main neuropathological markers of AD, although they are highly frequent in the brain of elderly people without the disease [3]. Amyloid or senile plaques result from the accumulation of beta-amyloid protein, one of the pathological hallmarks of AD. This protein is produced normally in the brain and evidence indicates that very small amounts are necessary to maintain neurons viable. The problem in AD is that its production is greatly increased and molecules accumulate as oligomers, resulting in synaptic changes, the first step in a series of events that lead to the loss of neurons and symptoms of the disease [4]. The objective of this review was to describe the presence of amyloid plaques and their consequence in AD.

Materials and Methods

This was a literature review of scientific studies that investigated the relationship between amyloid plaques and AD. The SciELO (Scientific Electronic Library Online) and PubMed databases were searched. The keywords were selected according to the descriptors of the DeCS site (Descritores em Ciências da Saúde - Descriptors in Health Sciences). Keywords addressing the topics amyloid plaques and AD and their English translations were thus chosen. National and international studies meeting some inclusion criteria were selected: only articles addressing the descriptors "placa amilóide e Doença de Alzheimer", "amyloid plaque AND Alzheimer disease" and " β -amyloid plaque OR Alzheimer disease", articles published after 1999, and articles published in English or Portuguese. Studies that did not meet these requisites were excluded. Human and experimental studies, as well as literature reviews, were included. Using this search strategy, 7 articles were included in this review. The full text of the articles was read to evaluate and discuss the main aspects reported in the studies regarding amyloid plaques and AD.

Results and Discussion

Amyloid plaques and intraneural neurofibrillary tangles involved in the alterations that occur in neuritic processes and

glial cells are the most important features of AD. The plaques are produced by brain deposits of fibrils of beta-amyloid peptide (A β), a fragment derived from the proteolysis of amyloid precursor protein (APP). This protein exhibits neurotoxic effects that compromise the life of neuronal cells and also induces intracellular changes that result in the formation of neurofilaments, contributing to the neurodegenerative process [5].

The processing of APP by alpha-secretase followed by gamma-secretase (amyloidogenic pathway) generates A β peptide fragments of 40 and 42 amino acids that have a high toxic potential. The 42-amino acid fragment is highly neurotoxic and its accumulation results in the formation of amyloid fibers and, subsequently, amyloid plaques. These fragments of APP, including A β , can exert a powerful regulation of basic neuronal functions such as cell excitability and synaptic transmission, and may also be related to the regulation of behaviors such as learning and memory [6]. Genetically, intracellular fragments of APP bind to transcription factors and are transported to the nucleus where they start to influence transcription. The regulation of APP proteolysis depends on the activity of a multimeric protein complex whose main components are presenilins [presenilin-1 (PS-1) and presenilin-2 (PS-2)]. Dominant mutations in these genes are found in most cases of early-onset familial AD, but account for less than 1% of all cases of AD [7].

According to the amyloid cascade hypothesis, the accumulation of A β is the main cause of degeneration and cognitive decline [8]. The mechanism of A β aggregation is divided into three stages. The first stage is characterized by the state of nucleation in which the conformation of A β changes from a random coil or α -helix to a β -sheet and the molecular state of A β promotes the formation of oligomers. The second stage is called the elongation phase, in which the nucleated A β gradually self-aggregates to form larger oligomers. The final stage is the stationary phase when the mature amyloid forms fibrils. The mechanism underlying the neurotoxicity induced by A β is complex and involves several apoptosis- or necrosis-associated

signaling pathways. Amyloid- β and its oligomers are able to rapidly block the mechanism through which new memories are formed, altering synaptic plasticity and its structure, with a consequent deficit in cognitive function, compromising postsynaptic transmission and modifying neuronal activity with the release of neurotoxic mediators by glial cells [9].

Conclusion

Amyloid plaques are important features in the development of Alzheimer's disease since their occurrence directly affects brain structures and functions.

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