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Alzheimer Diseases

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Alzheimer's disease (AD), the most common cause of dementia is accompanied by progressive memory loss and other cognitive functions. The conditionis estimated to affect approximately 36 million people, worldwide (1). AD is characterized by the presence of extracellular amyloid β (Aβ) deposits, intracellular neurofibrillary tanglesand senile plaques in the cortex, hippocampus, basal forebrain and amygdale (2). Neurofibrillary tangles formation is the result of intracellular fibrillar aggregation of the microtubule-associated protein tau that is hyperphosphorylated and oxidized. Senile plaques consist of insoluble fibrillar Aβ. It is established that Aβ is formed after sequential cleavage of amyloid precursor protein and secreted to the extracellular space. It also inhibits hippocampal long-term potentiation and disrupts the synaptic plasticity (3). In addition, Aβ accumulation induces an elevation in levels of reactive oxygen species (ROS) in neurons, leading to apoptotic neuronal death in rats and mice (4). Studies showed that the accumulation of Aβ in brain plays an important role in the pathophysiology of AD and a close correlation exits between Aβ procedure and the neurodegeneration process of AD (5). There exists evidence suggesting that memory impairment in AD begins with changes in hippocampal synaptic functions and then gradually progresses to neurodegeneration and neuronal loss in these patients (6).

The Aβ-induced damage in hippocampus might underlie some of the AD behavioral deficits. Long-term potentiation (LTP) is one of the most important forms of synaptic plasticity, linked to learning and memory (7). The Aβ makes changes in LTP, in the hippocampus and consequently impairs cognition and memory in rodents (3) and is widely reported to cause lipid peroxidation in brain cell membranes, leading to 4-hydroxy-2-nonenal (HNE) and acrolein formation, both toxic to neurons. These products alter the membrane protein conformation and eventually lead to neuronal death (8). The Aβ initiates free radical processes, resulting in protein oxidation, lipid peroxidation, ROS formation and cellular dysfunction, leading to calcium ion accumulation and subsequent neuronal death (9).

Pervious experimental studies have shown that Aβ (25-35) induce a wide pattern of central modifications, reminiscent of the human physiopathology, particularly short- and long-term memory deficit, oxidative stress, apoptosis, neuroinflammation, acetylcholine impairment, hippocampus alteration, tau hyperphosphorylation and amyloid burden (10). The deposition of β-amyloid protein in brain is related to learning impairment and cholinergic neuronal degeneration and the β-amyloid protein-treated rats could be used as AD animal models (11). The key brain regions, involved in the Morris water maze (MWM) task navigation, include the striatum, the frontal lobe and especially, the hippocampus (12).

The hippocampus structure has a key role in cognition and psychological function. Animal studies have shown that this structure is rapidly and extremely affected by an Aβ fragment injection (Aβ (25-35)) in rats, damaging the structure and function of the hippocampus (13, 14). The hippocampus plays an important role in contextual memory; the hippocampus injuries negatively affect the MVM task performance (15).

Nitta et al. showed that the water maze task performance was impaired in β-amyloid-treated rats, and the choline acetyl transferase activity significantly decreased in the frontal cortex and hippocampus (16). Therefore, the β-amyloid protein deposition in brain is believed to be related to learning impairment and cholinergic neuronal degeneration. It also means that β-amyloid protein-treated rats could be used as animal models for AD (11). Moreover, the studies indicated that intracerebroventricular (ICV) injection of Aβ (25-35), induced impairment in the passive-avoidance and redial-arm maze tasks, in the rat (11). Maurice confirmed the negative effect of ICV injection of Aβ (25-35) on learning in the Y-maze, passive avoidance and water maze tasks (17). The studies also reported

that bilateral injection of Aβ (25-35) induced learning deficits in passive- avoidance tasks, in rats (18). The hippocampus has an important role in spatial navigation and consolidation of information from short-term to long-term memory. Evidence have suggested that the memory impairment in AD begins with changes in hippocampal synaptic functions and progresses to neurodegeneration and neuronal loss in these patients (19). It has been reported that Aβ administration makes changes in LTP in the hippocampus and consequently leads to cognitive dysfunction and memory impairment in rodents (20). It is clear that oxidative stress plays a role in AD-induced neurotoxicity in the brain. The Aβ enters the bilayer neuronal membrane and generates oxygen-dependent free radicals, causing lipid and protein oxidation (21). Oxidative stress disrupts the blood brain barrier, leading to toxic substances passage to the brain and ultimately, resulting in the progression of various neurodegenerative diseases. Furthermore, the Aβ deposition activates the acute immune response of microglial cells and astrocytes, leading to production and activation of inflammation-related proteins, including complement factors and cytokines like interleukin-1, interleukin-6 and tumor necrosis factor-α and therefore leading to synaptic damage, neuronal loss and the activation of other inflammatory participants (9, 22, 23). As mentioned above, oxidative stress, following Aβ, involves development and progression of the AD. Brain is sensitive to oxidative stress, due to low antioxidant and cell membrane lipid levels (24). Oxidative stress reflects an imbalance between the systemic ROS manifestation and a biological system ability of detoxifying the reactive intermediate molecules or easily repairing the resulting damage.

Therefore, the use of an external antioxidant is one of the most common therapeutic strategies for neurotoxicity treatment. Several experimental studies have shown that dietary enrichment with nutritional antioxidant could improve brain damage and cognitive function (25-28).

A great number of different spices and aromatic herbs have been used as antioxidants in neurological diseases (29, 30).

Antioxidants that prevent the detrimental consequences of Aβ are consequently considered to be a promoting approach to brain neuroprotection in the AD (31).

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Authors' Contributions

S. Madadi gathered and wrote the manuscript and M. Mehdizadeh edited it.

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