IMPLICATION OF AGING RELATED FACTOR FOR PATHOGENIC MECHANISM IN ALZHEIMER'S DISEASE

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Pressure ulcers (pressure sores) continue to be a common health problem, particularly among the physically limited or bedridden elderly. The problem exists within the entire health framework, including hospitals, clinics, long-term care facilities and private homes. Following the global trend of population aging, China became an aging society at the end of the 20th century. The ever-growing medical demands of the elderly, the lag in medical insurance policy, and the late development of geriatric services make the present situation of public health in China worrying. Alzheimer's disease (AD), the most common form of dementia, is characterized by the presence of excessive deposits of aggregated amyloid-β (Aβ), which is derived from the amyloid-β protein precursor (APP) following processing by β- and γ-secretase. Metal elements are implicated in the pathophysiology of AD. Magnesium affects many biochemical mechanisms vital for neuronal properties and synaptic plasticity, and magnesium levels were reported to be decreased in various tissues including brain of AD patients. However, the exact role of magnesium in the neurodegenerative process of AD remains elusive. In this study, we investigated the effects of physiological, low, and high concentrations of extracellular magnesium ([Mg^{2+}] o) on APP processing and Aβ secretion. Here we show the effects of varying [Mg^{2+}] o on APP processing is time- and dose-dependent. After treatment, high [Mg^{2+}] o increased C-terminal fragment-α (CTFα) levels and soluble α-secretase cleaved APP (sAPPα) release via enhancing retention of APP on plasma membrane. In contrast, low [Mg^{2+}] o enhanced CTFβ accumulation and Aβ secretion, and reduced cell surface APP level. Varying [Mg^{2+}]o did not alter protein contents of full length APP. However, decreased total intracellular magnesium level by magnesium deprivation impaired cell viability. Normal APP processing could be restored when magnesium was adjusted back to physiological concentration. These data demonstrate that APP processing can be modulated by magnesium and at high [Mg^{2+}] o , APP processing favors the α-secretase cleavage pathway. Our findings suggest that supplementation of magnesium has a therapeutic potential for preventing AD.

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