Metformin a potential pharmacological strategy in late onset Alzheimer's disease treatment

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Abstract

Alzheimer's disease (AD) is one of the most devastating brain disorders. Currently, there are no effective treatments to stop the disease progression and it is becoming a major public health concern. Several risk factors are involved in the progression of AD, modifying neuronal circuits and brain cognition, and eventually leading to neuronal death. Among them, obesity and type 2 diabetes mellitus (T2DM) have attracted increasing attention, since brain insulin resistance can contribute to neurodegeneration. Consequently, AD has been referred to "type 3 diabetes" and antidiabetic medications such as intranasal insulin, glitazones, metformin or liraglutide are being tested as possible alternatives. Metformin, a first line antihyperglycemic medication, is a 5'-adenosine monophosphate (AMP)-activated protein kinase (AMPK) activator hypothesized to act as a geroprotective agent. However, studies on its association with age-related cognitive decline have shown controversial results with positive and negative findings. In spite of this, metformin shows positive benefits such as anti-inflammatory effects, accelerated neurogenesis, strengthened memory, and prolonged life expectancy. Moreover, it has been recently demonstrated that metformin enhances synaptophysin, sirtuin-1, AMPK, and brain-derived neuronal factor (BDNF) immunoreactivity, which are essential markers of plasticity. The present review discusses the numerous studies which have explored (1) the neuropathological hallmarks of AD, (2) association of type 2 diabetes with AD, and (3) the potential therapeutic effects of metformin on AD and preclinical models.

Author keywords

Alzheimer's disease; AMP activated protein kinase AMPK; Beta amyloid; Diabetes mellitus; Insulin resistance; Metformin; Tau protein hyperphosphorylation