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Insulin-degrading enzyme: Roles and pathways in ameliorating cognitive impairment associated with Alzheimer's disease and diabetes

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Alzheimer's disease (AD) and diabetes cognitive impairment (DCI) exhibit similar pathological characteristics, specifically the excessive accumulation of β-amyloid (Aβ) in the central nervous system (CNS). Insulin-degrading enzyme (IDE) is an enzyme of degrading both insulin and Aβ, prompting extensive investigation into the mechanisms through which IDE can improve these two cognitive disorders.

In terms of basic research, several potential mechanisms have been identified by which IDE improves AD and DCI. These mechanisms include increased expression of IDE in the CNS, facilitating the degradation of Aβ and thereby reducing its accumulation in the brain. Furthermore, IDE may ameliorate AD-related cognitive impairments by alleviating neuronal damage, suppressing excessive activation of glial cells, and inhibiting the excessive release of inflammatory factors. In relation to AD-related pathways, IDE may decrease the accumulation of Aβ in the CNS, subsequently improving AD-related cognitive impairments through activation of the PI3K/Akt/GSK3β, PPARγ, and AMPK pathways, or inhibition of the ERK/JNK/p38 MAPK and NF-κB pathways. Additionally, in the study of DCI, IDE may improve this condition by activating the PI3K/Akt/GSK3β pathway or inhibiting the Cdk5/p35 and cAMP/PKA pathways, and reducing Aβ accumulation and neuronal apoptosis in the brains.

In conclusion, considering the shared pathological characteristics of AD and DCI, as well as the involvement of IDE in Aβ degradation, IDE emerges as a promising therapeutic target for improving both conditions. We anticipate more innovative research findings regarding IDE in the treatment of AD and DCI, which will potentially expand the range of scientifically effective candidate drugs for clinical treatment.