Modulation of GLP-1 signaling as a novel therapeutic approach in the treatment of Alzheimer?s disease pathology

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Introduction: Clinical studies suggest a link between peripheral insulin resistance and cognitive dysfunction. Post-mortem analyses of Alzheimer disease (AD) subjects revealed insulin resistance in the brain, suggesting a role of this condition in cognitive deficits observed in AD. In this review, we focus on the glucagon-like peptide-1 (GLP-1) signaling pathway, whose role in the brain is collecting increasing attention because of its association with insulin signaling activation. Areas covered: The role of GLP-1-mediated effects in the brain and how they are affected along the progression of AD pathology is discussed. Furthermore, we provide a comprehensive discussion about the use of GLP-1 mimetics drugs, which have been developed as a treatment for T2DM but seem to possess a number of other physiological properties, including neuroprotective and anti-inflammatory effects, that may be useful to slow AD progression. Expert commentary: The repurposing of antidiabetic drugs for the modulation of brain insulin resistance in AD appears to be of great interest. The beneficial effects on synaptogenesis, neurogenesis, and cell repair as well as the reduction of the chronic inflammatory response, and most importantly the reduction of amyloid plaques in the brain indicate that these drugs have promise as novel treatments for AD.

Alzheimer disease

dementia

GLP-1

incretins

insulin resistance

antidiabetic agent

dipeptidyl peptidase IV inhibitor

glucagon like peptide 1

liraglutide

antidiabetic agent

glucagon like peptide 1

Alzheimer disease

amyloid plaque

antiinflammatory activity

cell regeneration

disease course

human

insulin resistance

nervous system development

neuroprotection

nonhuman

protein function

Review

signal transduction

synaptogenesis

Alzheimer disease

drug effects

metabolism

molecularly targeted therapy

signal transduction

Alzheimer Disease

Glucagon-Like Peptide 1

Humans

Hypoglycemic Agents

Insulin Resistance

Molecular Targeted Therapy

Signal Transduction