

IGSN - COLLOQUIUM

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Drugs developed to treat diabetes show neuroprotective effects in Alzheimer's and Parkinson's disease

Type 2 diabetes is a risk factor in the development of Alzheimer's disease (AD) and Parkinson's disease (PD). Importantly, insulin desensitisation has been observed in the brains of AD and PD patients. Incretin drugs such as Glucagon-like peptide-1 (GLP-1) and Glucose dependent Insulinotrophic Polypeptide (GIP) have been developed to treat type 2 diabetes. Long acting analogues of GLP-1 have shown very promising results in preclinical studies of AD and PD. The growth-factor signaling effects of incretins protect from oxidative stress, induce cell repair, promote stem cell activation, reduce apoptosis, and promote synaptogenesis and synaptic activity. GLP-1 and GIP analogues can readily cross the blood brain barrier, which set them apart from other growth factors. Another important aspect is that there are GLP-1 receptor agonists already on the market as a treatment for type 2 diabetes (liraglutide, Victoza[®], exendin-4, Byetta[®], lixisenatide Lyxumia[®]). We also have tested a range of analogues of Glucose dependent Insulinotrophic Polypeptide (GIP). These are effective in reducing the hallmarks of AD in an APP/PS1 mouse model. Amyloid plaque load, amyloid levels, synapse loss, oxidative stress and the chronic inflammation response was reduced in the brain. Memory formation and synaptic plasticity in the hippocampus was enhanced, as was neuroprogenitor proliferation and neurogenesis in the dentate gyrus. We also tested GLP-1 and GIP in the MPTP mouse model of Parkinson's disease. The drugs prevented the motor impairment induced by MPTP lesion, and rescued dopaminergic neurons in the substantia nigra while reducing chronic inflammation and apoptosis. Based on the encouraging pre-clinical evidence, several clinical trials are currently under way, testing liraglutide and exendin-4 in AD and PD patients. A clinical trial of liraglutide in AD patients showed good effects, and a larger trial is ongoing. A clinical trial of exendin-4 in PD patients showed very promising protective effects, including a clear improvement in the Mattis dementia rating scale. A trial testing liraglutide in PD patients has just started. Therefore, incretin analogues show great promise as treatments in neurodegenerative disorders.

Host:

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Guests are welcome