Studies on the plasticity of CNS cholinergic neurons

https://www.neurodegenerationresearch.eu/survey/studies-on-the-plasticity-of-cns-cholinergic-neurons/

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Canada

Title of project or programme

Studies on the plasticity of CNS cholinergic neurons

Source of funding information

CIHR

Total sum awarded (Euro)

€ 541,086

Start date of award

01/04/2013

Total duration of award in years

5.0

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords
Research Abstract

Our recent pharmacological studies revealed the existence of a group of enzymes in the brain responsible for the production and degradation of the protein Nerve Growth Factor (NGF). NGF is crucial for the “healthy” status of a group of neurons known as basal forebrain cholinergic neurons (BFCNs). These brain cells have key roles in learning and memory and are damaged in individuals with Alzheimer’s disease (AD). Previous investigations from our group showed that

the NGF pathway is affected in AD brains, so that NGF fails to mature and breaks down more quickly. These changes mean that there are reduced levels of NGF to BFCNs and explains how their degeneration occurs in AD. The present grant renewal aims to investigate whether this pathway is responsible for the “well-being” of BFCNs that contact NGF releasing areas. We propose that alterations in the NGF metabolic pathway exist in any situation where amyloid-beta (Abeta) peptides build up, as they do in AD. To test this, we will explore the NGF metabolic pathway in our rat model of AD and in the brains of Down’s syndrome (DS) sufferers. These people have an extra chromosome containing the gene expressing the precursor protein for the formation of Abeta (the peptide fragment central to AD development). Most DS individuals accumulate Abeta and develop AD by mid-life. We also want to investigate if the inhibition of molecules which break down NGF can reverse the deficits seen in AD. In these studies we will use our rats which mimic AD memory deficits. We will conduct a pharmacological investigation to test if cholinergic degeneration worsens AD pathology and if the use of drugs which protect the brain can delay onset of AD. Our investigations are important as it is estimated that a delay of 5 years in disease onset could reduce the incidence of AD by half.

Lay Summary
Further information available at:

Types:
Investments > €500k

Member States:
Canada

Diseases:
Alzheimer's disease & other dementias

Years:
2016

Database Categories:
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