Combined anti-inflammatory- and iron chelation therapy in a preclinical model of neurodegeneration with brain iron accumulation

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Contact information of lead PI Country

Denmark

Title of project or programme

Combined anti-inflammatory- and iron chelation therapy in a preclinical model of neurodegeneration with brain iron accumulation

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Lundbeckfonden

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€ 211,882

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01/11/2015

Total duration of award in years

3

Keywords

Research Abstract

The current project will examine the significance of anti-inflammatory therapy in combination with iron-chelation therapy in a pre-clinical model of neurodegeneration with brain iron accumulation (NBIA). Experimental animals (rats) are subjected to a controlled lesion in the

brain (the striatum) using stereotactic injection of glutamate, which leads to excitotoxicity and neuronal cell death in remote distance from the injection site due to glutamate toxicity (the substantia nigra pars reticulate) together with iron deposition and chronic inflammation. The experimental animals are treated with a GABA agonist (gaboxadol), iron-chelator (deferiprone), anti-inflammatory drugs (aminoguanidine, nimesulide), or combinations thereof. Their affection caused by the degenerative process is monitored in real time using MRI and scoring of motor performance. Post-mortem the substantia nigra pars reticulate is examined by stereological counting of neurons and macrophages, together with non-morphological measurement of iron and markers of oxidative damage in dissected ventro-lateral portions of the mesencephalon. Mechanistic studies are performed in cultured primary neurons subjected to glutamate and co-cultured with macrophages. It is expected that the studies can provide significant conclusions on the usage of iron-chelators and anti-inflammatory drugs for treatment in experimental NBIA.

Further information available at:

Investments < €500k
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