

Amyloid and vessels: Imaging the role of cerebrovascular function

<https://neurodegenerationresearch.eu/survey/amyloid-and-vessels-imaging-the-role-of-cerebrovascular-function/>

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Netherlands

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Amyloid and vessels: Imaging the role of cerebrovascular function

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NWO

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5.0

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Research Abstract

Cerebral amyloid angiopathy (CAA) is a disease characterized by amyloid deposits in cortical arteries and arterioles, leading to brain haemorrhages and cognitive decline. CAA is common in the elderly, but also occurs in a hereditary form, cerebral hemorrhage with amyloidosis-Dutch type (HCHWA-D). Though the disease occurs in brain vessels, the interaction between vascular dysfunction and amyloid accumulation is not clearly understood. In this project I want to study

this interaction by addressing the following questions:

- 1) What are the vascular and inflammatory changes caused by amyloid accumulation in the vessel wall?
- 2) Are these changes different for the HCHWA-D mutation of the amyloid-beta peptide, which causes accelerated amyloid deposition?
- 3) Does improvement of vascular function or the inflammatory response using existing approved drugs lead to improved vessel function, delay in amyloid angiopathy, and a reduction of microbleeds and cognitive decline?

To answer the first question, I will use in vivo MRI measurements of brain perfusion and vascular reactivity in animal models of CAA, to assess vascular dysfunction with increasing amyloid load, and correlate these data to structural MRI, occurrence of microbleeds and to cognition. In the same mouse models, I will use intravital microscopy of cortical arterioles to elucidate the direct interaction of amyloid accumulation with endothelial activation and smooth muscle cell function at the level of individual vessels.

For the second question, we will determine the vascular pathologies associated with amyloid accumulation in post-mortem human brain material for sporadic CAA, and for HCHWA-D patients. Based on these results, I will select anti-inflammatory or anti-angiogenic drugs to test their effect on the progression of vascular amyloid deposits, vascular function, and improved cognition and occurrence of microbleeds.

Ultimately, this research should lead to a clinical trial with these approved drugs in patients with HCHWA-D, or a diagnosis of probable CAA.

Lay Summary

Further information available at:

Types:

Investments > €500k

Member States:

Netherlands

Diseases:

Alzheimer's disease & other dementias

Years:

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