Are levels of brain miRNA specifically linked to neuroinflammation and synaptic plasticity altered in relation to pathological mechanisms characteristic of AD?

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Research question and background

miRNAs are small molecules produced from a particular set of genes that do not produce a protein but rather control cellular function as an RNA molecule. In the hippocampus these molecules are key actors in controlling learning and memory and influence a number of cellular processes relevant to hippocampal functions like synaptic plasticity, dendritic branching, adult neurogenesis and neuronal survival. miRNA are also implicated in the regulation of inflammatory responses and have been suggestsed to be involved in several neuropathological mechanisms. Indeed, studies on CSF and brain tissue from Alzheimers diseaese (AD) patients show alterations in expression of various miRNA regulating inflammatory signaling, amyloid precursur protein (APP) expression and neurodegeneration. In the current study we aim to investigate whether levels of brain miRNA specifically linked to neuroinflammation and synaptic plasticity is altered in relation to pathological mechanisms characteristic of AD. By doing so we hope to identify miRNAs as potential biomarkers as well as to find novel disease-related miRNAs.

Methods and tissue

We will extract total RNA from brain tissue samples, hippocampus and temporal lobe cortex (preferably medial) as well as internal control tissue (cerebellum) from both AD patients and non-demented controls. The RNA will be analyzed using RNA-deep sequencing. In order to further correlate AD pathology to potential changes in miRNA levels and biogenesis, we will by the use of different ELISA assays analyse levels of biomarkers (including Aβ1-42, cytokines, chemokines and glial cell specific activity markers such as NG2, YKL40 and GFAP) in homogenates of brain tissue adjacent to tissue extracted for miRNA deep sequencing.

Results and conclusion

Understanding how miRNAs are linked to the pathological changes seen in AD patients will add an additional dimension to the current knowledge of underlying mechanisms causing cognitive malfunctions. The long-term goal of the proposed study is to evaluate whether miRNAs could serve as early biomarker for AD as well as targets in future drug discovery trials for new AD treatment strategies.
Analysis of the tissue has not yet started.