Using functional cell studies to characterize and map the sensitivity and response to pathology-associated agents of various post-mortem isolated primary human glial cell cultures

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Research question and background

An increasing number of studies have described neuroinflammatory events in patients with neurodegenerative disorders such as Alzheimers disease (AD) and synucleinopathies. Neuroinflammation in these disorders is suggested to in part be triggered by disease-related accumulation of aggregated proteins in the brain. In patients with synucleinopathy like Parkinson's disease and dementia with Lewy bodies the aggregations are foremost represented by intracellular α-synuclein inclusions whereas AD patients display extracellular accumulation of the amyloid beta (Aß) peptide (senile plaques) and intraneuronal tangles of hyperphosphorylated tau. The key players in neurodegeneration-associated neuroinflammatoin are glial cells which become activated and secrete inflammation-modulating factors in brain areas containing pathological protein aggregations. These neuroinflammatory processes can be monitored in cerebrospinal fluid (CSF) and several recent studies have indeed described alterations in the levels of various inflammatory molecules in the CSF of patients with neurodegenerative disorders. The cellular mechanisms underlying these altertions need to be investigated in systems closely resembling the situation in the human brain, preferably in primary human tissue culture systems. However, most published literature on glial cell involvement in neurodegeneration describes results obtained from rodent cultures and confirming results from primary human cell cultures are scarce. Additionally, most published studies on primary human cells are performed on cells isolated from fetal tissue and the need for repetition and extension of these studies in cultures isolated from human adult brain to further investigate mechanisms of glial cell activation in these disorders , is undisputable.

Methods and tissues used

In the current project we therefore aim to use functional cell studies to characterize and map the sensitivity and response to pathology-associated agents of various post-mortem isolated primary human glial cell cultures.

Samples from the white matter, hippocampus, entorhinal cortex, brain stem, cerebellum, gyrus angularis as well as cerebrospinal fluid are currently collected from AD, PD, PDD, DLB, MS patients and non demented controls. The cell cultures (astrocytes, NG2 cells and pericytes) will be isolated using optimized established protocols. Cellular responses will be analyzed using immunocytochemistry, enzyme-linked immunosorbent assay (ELISA), Flow cytometry and live cell imaging.

Results and conclusion

We have isolated pericytes from 6 nondemented controls and 1 AD patients, but have not performed any experiments and has thus not published any papers.