

Establish a human *in vitro* model mimicking grey matter MS pathology

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Research question and background

Multiple sclerosis (MS) is characterized by inflammation-driven demyelination and extensive grey matter pathology in the central nervous system (CNS). Cortical pathology is characterized by severe demyelination and neuroinflammatory processes, including microglial activation, meningeal inflammation, oxidative damage and neuronal mitochondrial dysfunction. Despite extensive research still little is known how these processes contribute to neurodegeneration. This unfortunate situation is mainly caused by the lack of experimental *in vitro* models that reproduce important aspects of MS cortical pathology, indicating the need for alternative models. The aim of this proposal is to establish and validate an experimental human *in vitro* model that accurately reproduces key aspects of cortical MS pathology.

Methods and tissues used

We have now set up a human organotypic slice culture system using cortical brain tissue from non-neurological patients or patients with minimal cortical pathology with a short post-mortem delay time.

Results and conclusion

Our preliminary data shows that cortical slices can be cultured for several days and contain a large number of viable neurons. Moreover, we show that slice cultures exposed to proinflammatory cytokines exhibit microglial activation and mitochondrial defects. In future, we aim to induce demyelination using the bioactive lipid lysophosphatidylcholine, which is known to cause demyelination in rodent slice cultures. In future, this experimental *in vitro* model will allow us to elucidate and therapeutically modulate cellular and molecular pathways that contribute to cortical demyelination and neurodegeneration in MS in a human setting.