Small vessel disease pathophysiology: human post-mortem brain tissue study with clinical-radiological-pathological correlation

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Alzheimer's Society

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Small vessel disease pathophysiology: human post-mortem brain tissue study with clinical-radiological-pathological correlation

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The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords
Research Abstract
Human small vessel disease (SVD) is a common pathological process, causing up to 45% of

dementias and 20% of all strokes. The pathophysiology of SVD is poorly defined, until recently believed to be an extension of large vessel atherosclerosis. Our clinical and neuroimaging human-to-experimental translational studies suggest that SVD is multifactorial, with subtle defects affecting most of the neurovascular unit.
This study will re-translate the experimental model findings back to humans, interrogating the neurovascular unit to assess key pathways thought to underlie SVD. We will use brain tissue from three highly phenotyped cohorts within the MRC Edinburgh Brain Bank, representing mild to severe SVD. High field MR imaging of tissue blocks will be followed by histology and immunohistochemical study with image analysis quantification. Laser capture microdissection of individual neurovascular units will be performed for gene array procedures and pathway analyses. Precise clinical-radiological-pathological correlations will then be performed. Collaboration with the Cognitive Function and Ageing Study will facilitate replication and enhance the generalisability of results.
We will also work with other neuropathology experts to refine and standardise grading systems for human microvascular pathology. This will form the basis of a proposed international collaborative workshop to develop SVD standards and harmonise neuropathology terminology.
This study will enable us to better understand why and how human SVD develops and if there are identifiable factors that make individuals more susceptible to it. This information will inform future research to identify potential therapeutic and preventative targets

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