Lay Summary

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CAA and dystroglycanopathies

Dr Roxana Carare, University of Southampton

Research has implicated the basement membrane (BM) in the route for the perivascular elimination of amyloid-β, the failure of which is believed to contribute to Alzheimer's disease (AD) pathogenesis. Collagen IV is a ubiquitous BM component with structural and functional roles. Laminin connects collagen IV to the dystrophin glycoprotein complex (DGC), a transmembrane structure essential for embryonic BM development. In the human brain the DGC is located in perivascular astrocyte end-feet where it acts as an anchor to aquaporin 4 (AQP4), a water channel reported to aid elimination of toxins such as amyloid-β from the brain via convective bulk flow.

Dystroglycanopathies are a clinically heterogenous group of muscular dystrophies caused by an abnormality with the α-dystroglycan component of the DGC. Dystroglycanopathies are used in this study as a model of disrupted BMs to explore their potential for use in future AD research where the analysis of amyloid-β along compromised BMs is valuable. Additionally, the literature is currently lacking an understanding of how the DGC influences the development of collagen IV in cerebrovascular BMs.

This study investigates how the general morphology and contours of vessels is altered in dystroglycanopathies in human brain tissue by immunohistochemical staining for collagen IV and will involve a quantitative comparison of both staining and blood vessel diameter between dystroglycanopathies and normal tissue. Dystroglycanopathies exhibit observably weaker staining and a statistically significant greater blood vessel diameter with a mean difference of 3.17um (2.72, 3.62, $P<0.001$), possibly due to a thickened BM. It was observed that dystroglycanopathy BMs appear to be more rugged and tortuous indicating structural irregularities which may result in a functional deficit.