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COMPLEMENT ACTIVATION IN MS: AN IMMUNOHISTOCHEMICAL ANALYSIS

Gillian Ingram,¹ Samantha Loveless,¹ Owain Howell,² Svetlana Hakobyan,¹
Bethan Dancey,¹ Neil Robertson,¹ James Neal,¹ Paul Morgan¹. ¹*Cardiff University;*
²*Swansea University*

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Activation of the complement cascade is clearly implicated in the pathology of multiple sclerosis (MS). However, the extent and nature of its involvement in specific pathological processes remains uncertain.

We describe a detailed immunohistochemical study to localise a strategically selected set of complement proteins, activation products and regulators in brain and spinal cord tissue of 17 patients with progressive MS, examining 35 different plaques, and 16 control donors, including 9 with CNS disease.

Plaques were consistently positive for complement proteins (C3, factor B, C1q), activation products (C3b, iC3b, C4d, TCC) and regulators (factor H, C1-inhibitor, clusterin), suggesting continuing local complement synthesis, activation and regulation despite no other evidence of on-going inflammation. Complement immunolabelling was most apparent in plaque and peri-plaque areas but also present in normal appearing white matter and cortical areas to a greater extent than in control tissue. Cellular staining for complement components was largely restricted to reactive astrocytes, often adjacent to clusters of microglia in close apposition to complement opsonised myelin and damaged axons.

These findings demonstrate the ubiquity of complement involvement in MS, imply a pathological role for complement in myelin and axonal damage and make the case for targeting complement in progressive phases of MS.