

DIFFERENTIAL LOCALISATION AND EXPRESSION OF COMPLEMENT IN A RAT MODEL OF MOTOR NEURON DISEASE

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The complement system is a key component of the innate immune system that has recently been implicated in numerous neurodegenerative pathologies, including Huntington's disease and Motor Neuron Disease (MND; Woodruff et al., 2006). However, the extent to which complement activation subserves neuroprotective or neurodegenerative functions in these pathologies is controversial. Here we report that in a transgenic rat model of MND – which expresses a toxic gain-of-function mutation of the human superoxide dismutase one (SOD1) gene – there is differential localisation and expression of key components of the complement cascade, including C5a, C3 and the Membrane Attack Complex (MAC). C5a has been of particular interest as a recent study showed that preventing C5a signalling by means of C5a receptor (C5aR) antagonist application was able to significantly attenuate both neurodegeneration and disease progression in a rat model of Huntington's disease (Woodruff et al., 2006b). In addition, it has been found that application of C5aR antagonists in SOD1 rats delayed both the onset and severity of MND with improved lifespan and weight (Woodruff et al., 2006a). Consequently, we are currently investigating the expression levels of C5aR in motor neuron pools of wildtype and SOD1 transgenic rats. To date we have observed altered C5aR, C3 and MAC expression and localisation between wildtype and SOD1 rats on motor neurons, astrocytes, and microglia using immunofluorescence. We are currently consolidating these findings with mRNA and protein expression experiments. These results, together with the previous finding that C5aR antagonists can significantly decrease neuromotor symptoms in SOD1 rats, strongly support further investigation into complement and C5aR inhibitors as potential therapeutics for alleviating the symptoms of MND.