Introduction: A complex relationship exists between astrocytes and neurons involving astroglial uptake of glucose, glutamate and glutathione precursors and the release of lactate, glutamine and glutathione, which are in turn taken up by neurons. This metabolic exchange occurring between astrocytes and neurons is vital to normal neuronal functions such as energy metabolism, glutamatergic signalling and GSH-dependent cellular defence. We hypothesise that a breakdown in astroglial-neuronal interaction, due to inflammation-activated astrocytes altering their phenotype, could lead to neurodegeneration, as observed in Alzheimer’s disease.

Aim: To investigate and attempt to reverse the affect of inflammatory activation on the neurosupportive functions of astrocytes.

Methods: U373MG human astrocytes were activated up to 120 hours using various concentrations of IL-1β and TNF-α. Levels of glucose, lactate, glutamate, glutathione and related thiols were measured in the conditioned media to determine how activation affects three important neurosupportive functions of astrocytes.

Results: Activated astrocytes show numerous time and cytokine concentration dependent changes in their neurosupportive functions. Most notably, chronically activated astrocytes significantly decrease glucose (40%) and glutamate (5%) uptake, decrease lactate (90%) and glutathione release (90%) and increase production of neurotoxic substances such as IL-6 (400%) and homocysteine (200%). Immunohistochemical co-culture studies and astrocyte-targeted interventions demonstrate the detrimental affect that inflammation-induced modulation of astroglial phenotype has on neuronal viability.

Conclusion: Inflammation-induced changes in astroglial neurosupportive functions are believed to play a role in neurodegeneration observed in Alzheimer’s disease. Therefore, our findings enable us to suggest evidence-based astrocyte-targeted therapeutic approaches for the treatment of Alzheimer’s disease.