Astrocytes are star-shaped cells and among the most abundant and versatile cell types in the central nervous system (CNS). We are only just beginning to understand the importance of this cell type in normal brain homeostasis and consequently little is known about its role in neurological diseases. Multiple sclerosis (MS) is a chronic inflammatory disease, characterized by focal accumulation of immune cells, which form demyelinated lesions throughout the CNS. Generally MS patients initially suffer from periods of neurological deficits followed by recovery. Over time, these neurological deficits can become progressive and permanent. This progression is thought to be the result of increasing loss of neurons in MS patients. Current therapies for MS are aimed at repressing the immune system, which is effective to limit the initial neurological deficits, but do not affect the ongoing neurodegeneration and MS progression. Previous studies indicated that MS progression is likely caused by ongoing local inflammation in the brain, associated mitochondrial dysfunctional and neurodegeneration. Therefore, new therapeutic approaches should aim to limit CNS inflammation and improve metabolic function and repair. In this thesis we elucidated novel mechanisms by which astrocytes can affect neuroinflammation and neuronal function. In this thesis we show that astrocytes are star players in metabolic regulation, redox handling and controlling local inflammation. We demonstrated that astrocytes play a cardinal, but dual, role in both neurodegenerative and neuroinflammatory processes and as such represent an interesting target for therapeutic intervention in MS.