Cellular distribution of glucose and monocarboxylate transporters in human brain white matter and multiple sclerosis lesions

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To ensure efficient energy supply to the high demanding brain, nutrients are transported into brain cells via specific glucose (GLUT) and monocarboxylate (MCT) transporters. Mitochondrial dysfunction and altered glucose metabolism are thought to play an important role in the progression of multiple sclerosis (MS). Here we investigated the cellular localization of key GLUT and MCT proteins in human brain tissue of non-neurological controls and MS patients. We show that in control brain tissue GLUT and MCT proteins were abundantly expressed, particularly in microglia and endothelial cells. In active MS lesions GLUTs and MCTs were highly expressed in reactive astrocytes. Astrocytes manifest increased MCT1 staining and maintain GLUT expression in inactive lesions, whereas demyelinated axons exhibit significantly reduced GLUT3 and MCT2 immunoreactivity in inactive lesions. Finally, we demonstrated that the co-transcription factor peroxisome proliferator-activated receptor gamma co-activator 1-alpha (PGC-1α), an important protein involved in energy metabolism, is highly expressed in reactive astrocytes in active MS lesions. Overexpression of PGC-1α in astrocytes increased GLUT and MCT proteins. In conclusion, we provide for the first time a comprehensive overview of key nutrient transporters in white matter brain samples. Moreover, our data demonstrate an altered expression of these nutrient transporters in MS brain tissue, including a marked reduction of axonal GLUT3 and MCT2 expression in inactive lesions, which may impede efficient nutrient supply to the hypoxic demyelinated axons thereby contributing to the ongoing neurodegeneration in MS.