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DIFFERENTIAL EXPRESSION OF TRANSLOCATOR PROTEIN (TSPO) IN MULTIPLE SCLEROSIS REFLECTS ACTIVATED MICROGLIA AND ASTROCYTES

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Microglia are the resident immune cells of the central nervous system. A frequently used marker for *in vivo* activated microglia is the 18kDa translocator protein (TSPO). TSPO is widely used as a Positron Emission Tomography (PET) imaging target to visualize injured brain areas and microglial activation. TSPO, formerly known as the peripheral benzodiazepine receptor, is a cholesterol binding protein localized to the outer mitochondrial membrane. Despite the proposed roles of TSPO, little is known about the cells expressing TSPO, namely the microglia and astrocytes, in neuroinflammatory and neurodegenerative disorders. However, localisation of TSPO in relation to lesions and cell types is unknown. Therefore, we performed immunohistochemistry on brain tissue containing different white and grey matter. Multiple sclerosis (MS) lesions (n = 56) were compared with brain tissues from healthy controls (n = 10) to determine expression of TSPO. Low levels of TSPO expression were found in the white matter of healthy controls (16.9±2.4%) and normal appearing white matter (NAWM) (22.9±16.4%) in MS cases. Conversely, significantly increased levels of TSPO expression were observed in microglia of active white matter lesions (12.9±7.5%) and the rim of chronic active lesions (15.1±8.5%) in MS cases compared to controls (1.2±0.6%) and NAWM (0.7±0.8%). Furthermore, TSPO was also found to be expressed in astrocytes at the centre of active lesions. These findings show the localisation of TSPO in MS lesions in the brain and highlight that PET imaging using TSPO ligands in people with MS not only reflects microglia and macrophage activity *in vivo* but also the response of astrocytes, as well as cells of the adaptive immune response.

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