The role LXR α in myelin debris clearance during demyelinating conditions

During acute demyelination, microglia and macrophages clear myelin debris by phagocytosis and thus promote repair and remyelination. Myelin has high lipid content, and thus during demyelinating condition microglia/macrophages are confronted with a high volume of lipid that it must clear. Little is known about the effect of lipid accumulation in microglia/macrophages on repair and remyelination. As previous literature suggests that LXR α-knockout mice have deficits in lipid efflux and transport out of cells, we used LXR α-knockout mice to study an artificial system of microglia/macrophages with a lipid overload phenotype, during demyelination. In order to do so, we induced unifocal demyelination using lysolecithin injection in wild type and LXR α-knockout mice. We then immunostained brain slices from these two genotypes with markers for myelin (fluoromyelin), lysosomes (Lamp1), lipid droplets (LipidTox), microglia/macrophages (Iba1) and the activation states of microglia/macrophages (iNOS and Arginase-1) 4 days and 21 days post-injection. While the initial degree of demyelination, lysosomal accumulation, microglial infiltration and inflammation (marked by iNOS) were perfectly comparable between the two genotypes at 4 days, there was significantly less remyelination, more lysosomal accumulation, more microglial infiltration and more inflammation in the LXR α-knockout mice compared to the wild type, 21 days post injection. In conclusion, our results indicate that deficiencies in lipid efflux affect efficient remyelination after an acute demyelinating event in the CNS.