**Examining the microglial TSPO phenotype in Alzheimer’s disease**

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**Background:** Neuroinflammation is a key pathological feature of Alzheimer’s disease (AD), with microglia being the main inflammatory cell type in the CNS. In order to examine these cells in vivo, PET ligands targeting the microglial translocator protein (TSPO) have been developed. However, it remains unclear the specific target of these ligands, whether this is all microglia or a subset of cells. We aim to elucidate this by identifying the microglial phenotype most associated with TSPO in humans.

**Method:** Human post-mortem sections of temporal lobe (TL) and cerebellum (Cb) from cases classified by Braak stage (0-II, III-IV, V-VI; each n = 10) were immunostained for pan-Aß, pTau, and microglial markers TSPO, Iba1 and HLA-DR with protein load quantified. Double immunofluorescent staining was performed with TSPO and microglial markers HLA-DR and CD68 with positive cells counted.

**Result**: TL showed an increase in Aβ (P<0.0001), pTau (P<0.0001) and TSPO (P<0.0001) protein load, but not Iba1 or HLA-DR, with progressing Braak stage. Aβ (P = 0.0008) and Iba1 (P = 0.012) load increased in the Cb, but not pTau, TSPO or HLA-DR. Of note, TSPO load in TL was associated with pTau. In both areas, no difference was found in number of HLA+ or CD68+ cells, though TL TSPO+ cell number increased significantly (P = 0.0347). There was no difference in the number of HLA-DR+/TSPO+ or CD68+/TSPO+ cells with progressing Braak stage. However, significantly more CD68+/TSPO+ than HLA-DR+/TSPO+ cells were detected in both the TL (P<0.0001) and Cb (P = 0.009) regions.

**Conclusion:** The results suggest that TSPO expression is related to late stage disease (pTau) and microglial phagocytosis (CD68), a function we have previously identified associated with the presence of dementia, cognitive decline and tau pathology. Further additional analysis with other microglial markers is currently ongoing.