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The immune system in Frontotemporal lobar degeneration with tau

Frontotemporal lobar degeneration with tau (FTLD-tau) is a group of tauopathies that underlie ~50% of cases of frontotemporal dementia (FTD). The discovery of genetic risk variants related to innate/adaptive immunity have highlighted a potential role for neuroinflammation in FTLD. Furthermore, studies have shown microglial and astrocyte activation together with T cell infiltration in the brain of THY-Tau22 tauopathy mice.
We investigated the relationship between tau and the immune system in human post-mortem brain tissue from 12 FTLD-MAPT, 33 Pick's disease, 45 Progressive Supranuclear Palsy patients and 55 controls. Using immunohistochemistry, we assessed tau pathology, the immunophenotype of microglia and astrocytes and the presence of infiltrating T cells.
Tau epitopes (Tau-2, AT8, AT100, CP13, Thr181, Ser356, Ser396, and PHF1) were increased in FTLD-Tau. Out of the six microglial markers (Iba1, CD68, HLA-DR, CD64, CD32a and CD16) only CD16 was increased in FTLD-MAPT. No change was observed in FTLD-Tau with the pan-astrocytic marker ALDH1L1 while GFAP expression was increased and the markers of astrocytes glutamate cycling function EAAT2 and glutamine synthetase reduced. Finally, CD4 and CD8 T lymphocytes were recruited in the brain parenchyma as part of the disease.
Our findings suggest a more important role for astrocytes than microglia in FLTD-tau and support the involvement of T lymphocytes in the pathogenesis of FTLD-tau.