

Microglial phenotypes and toll-like receptor 2 in the substantia nigra and hippocampus of incidental Lewy body disease cases and Parkinson's disease patients.

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(see also overlap with projects from Van Dam, vdBerg, Swaab)

Next to α -synuclein deposition, microglial activation is a prominent pathological feature in the substantia nigra (SN) of Parkinson's disease (PD) patients. Little is known, however, about the different phenotypes of microglia and how they change during disease progression, in the SN or in another brain region, like the hippocampus (HC), which is implicated in dementia and depression, important non-motor symptoms in PD. We studied phenotypes and activation of microglia in the SN and HC of established PD patients (Braak PD stage 4–6), matched controls (Braak PD stage 0) and of incidental Lewy Body disease (iLBD) cases (Braak PD stage 1–3) that are considered a prodromal state of PD. As recent experimental studies suggested that toll-like receptor 2 (TLR2) mediates α -synuclein triggered microglial activation, we also studied whether TLR2 expression is indeed related to pathology in iLBD and PD patients. A clear α -synuclein pathology-related increase in amoeboid microglia was present in the HC and SN in PD. Also, morphologically primed/reactive microglial cells, and a profound increase in microglial TLR2 expression were apparent in iLBD, but not PD, cases, indicative of an early activational response to PD pathology. Moreover, TLR2 was differentially expressed between the SN and HC, consistent with a region-specific pattern of microglial activation. In conclusion, the regional changes in microglial phenotype and TLR2 expression in primed/reactive microglia in the SN and HC of iLBD cases indicate that TLR2 may play a prominent role in the microglial-mediated responses that could be important for PD progression.