Proliferation in the Alzheimer hippocampus

Lucassen, P.J., SILS-CNS, University of Amsterdam, the Netherlands.
(see also overlap with projects from Van Dam, vdBerg, Swaab)

Microglia and astrocytes contribute to Alzheimer's disease (AD) etiology and may mediate early neuroinflammatory responses. Despite their possible role in disease progression and despite the fact that they can respond to amyloid deposition in model systems, little is known about whether astro- or microglia can undergo proliferation in AD and whether this is related to the clinical symptoms or to local neuropathological changes. Previously, proliferation was found to be increased in glia-rich regions of the presenile hippocampus. Since their phenotype was unknown, we here used two novel triple-immunohistochemical protocols to study proliferation in astro- or microglia in relation to amyloid pathology. We selected different age-matched cohorts to study whether proliferative changes relate to clinical severity or to neuropathological changes. Proliferating cells were found across the hippocampus but never in mature neurons or astrocytes. Almost all proliferating cells were co-labeled with Iba1+, indicating that particularly microglia contribute to proliferation in AD. Proliferating Iba1+ cells was specifically seen within the borders of amyloid plaques, indicative of an active involvement in, or response to, plaque accumulation. Thus, consistent with animal studies, proliferation in the AD hippocampus is due to microglia, occurs in close proximity of plaque pathology, and may contribute to the neuroinflammation common in AD.