Does innate immunity contribute to Alzheimer's disease?

Accumulation of neurotoxic amyloid-β peptides along with neurofibrillary tangle formation represent key pathological hallmarks in Alzheimer's disease (AD). Despite the brain being viewed as an immune privileged organ, increasing evidence from translational, genetic and pathological studies suggests that activation of distinct innate immune pathways represents a third important component, which, once initiated, actively contributes to disease progression and chronicity. Microglia play a pivotal role in this immune response and are activated by binding of aggregated proteins or aberrant nucleic acids to pattern recognition receptors. This immune activation leads to the release of inflammatory mediators but also distracts microglia cells from their physiological functions and tasks. NLRP3 inflammasome activation and release of ASC specks contribute to spreading of pathology and impairs microglia clearance mechanisms together contributing to neuronal degeneration and spatial memory deficits. In keeping with this, inhibition of this immune pathways shows protection in cellular and murine models of AD. Modulation of the microglia driven innate immune response at key signalling steps may therefore provide protection and may alter progression of disease. Therefore, anti-inflammatory treatment strategies should be considered. Data on microglial activation in AD along with suggestions to modify and alter the pro- into an anti-inflammatory phenotype will be reviewed and discussed.

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