



Contributions of A β and Tau to Neuroinflammation and Cognitive Decline: Insights from 3xTg-AD and hTAU Mouse Models

Poster

Neurobiología de enfermedades - Neurobiology of disease

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Alzheimer's disease (AD) is a neurodegenerative disorder, characterized by cognitive decline, Abeta plaques deposition, intracellular neurofibrillary tau tangles (NFT) and chronic neuroinflammation. Evidence suggests that neuroinflammation is not merely a secondary response but an active driver of disease progression, making it a critical target for early diagnosis/therapeutic intervention.

This study aims to characterize the neuroinflammatory and neurodegenerative profile in the 3xTg-AD and the hTau-tauopathy mice models. The 3xTg-AD combines mutant hAPP (Swedish), PSEN1 (MM146V) and tau (P301L) transgenes recapitulating A β and tau pathologies in brain regions associated with AD; meanwhile, htau mice express full length wild-type human MAPT transgene, producing an aberrant content of tau isoforms. By comparing 3xTg-AD, which replicates full AD, with hTau that isolates tau pathology, we aim to disentangle the individual contributions of A β and tau to neuroinflammation and cognitive decline.

We integrated PET/MRI imaging for brain metabolism analysis with histological, biochemical and behavioral assessment in mice during their lifespan. We observed that in 3xTg-AD, cognitive deficits emerge at 3-6 months, preceding detectable cortical alterations on PET/MRI, which become more prominent at later stages of the disease. Histological findings indicated that the subiculum is a major site of pathology, in which Abeta deposition, NFT and reactive astrocytes were evidenced. In the hTau model, cognitive deficits were observed from 6-months onwards, followed by a progressive hypometabolism in the medial prefrontal cortex, detectable from 6-to-9 months-old, which became more pronounced at 12-months. Ongoing work aims to describe the inflammatory processes involved across both experimental models.

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