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Amyloid-β Oligomers, Neuroinflammation and Novel Targets for Alzheimer's Disease

Michael Harte
University of Manchester, United Kingdom

With current treatments for Alzheimer's disease (AD) only providing temporary symptomatic benefits disease modifying drugs are urgently required. This approach relies on improved understanding of the early pathophysiology of AD.

A new hypothesis has emerged, in which early memory loss is considered a synapse failure caused by soluble amyloid-β oligomers (Aβo). These small soluble Aβo, which precede the formation of larger fibrillar assemblies, may be the main cause of early AD pathologies. In support of this we have previously demonstrated the effects of an acute administration of LMW Aβo (SynAging) on cognitive, inflammatory, synaptic and neuronal markers in the rat [Watremez et al., 2018 Journal of Alzheimer's Disease]. This model is very well established in our lab, is robust, reproducible and gives a measurable cognitive end point within 2 weeks. We have utilised this model for assessing symptomatic and/or neuroprotective effects of disease modifying drug candidates.

It is becoming apparent that one such target, inflammation, is a key contributor to the progression of AD. In particular, on-going research is establishing the NLRP3-inflammasome complex as one of the most important regulators of inflammation, and that NLRP3 is central to the development of inflammation, pathology and memory deficits in rodent models for AD research. Our data point toward the NLRP3 inflammasome as a novel therapeutic target for AD.

Biography:

Michael Harte is a neuropharmacology researcher currently working in the Division of Pharmacy & Optometry at the University of Manchester as a Senior Lecturer in Drug Action. Her lab specialises in the development of preclinical models of neuropsychiatric and neurodegenerative disorders for the testing of novel compounds for progression to the clinic. Her overall research goal is to develop improved preclinical models to advance our understanding of different CNS diseases and aid in the identification and testing of novel targets to ultimately improve treatment for patients.