Title: Role of Tau in chromatin remodeling and gene expression

Abstract: Neuronal hyperexcitability linked to an increase in glutamate signalling is a peculiar trait of the early stages of Alzheimer's disease (AD) and tauopathies, however, a progressive reduction in glutamate release follows in advanced stages. We recently reported that in the early phases of the neurodegenerative process, soluble, non-aggregated Tau accumulates in the nucleus and modulates the expression of disease-relevant genes directly involved in glutamatergic transmission, thus establishing a link between Tau instability and altered neurotransmission. We observed that while the nuclear translocation of Tau in cultured cells is not impaired by its own aggregation, the nuclear amyloid inclusions of aggregated Tau abolish Tau-dependent increased expression of the glutamate transporter. Remarkably, we observed that in the prefrontal cortex (PFC) of AD patient brain, the glutamate transporter is upregulated at early stages and is downregulated at late stages. The Gene Set Enrichment Analysis indicates that the modulation of Tau-dependent gene expression along the disease progression can be extended to all protein pathways of the glutamatergic synapse. Together, this evidence links the altered glutamatergic function in the PFC during AD progression to the newly discovered function of nuclear Tau.

References:
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