TAU ENHANCES A-SYNUCLEIN AGGREGATION IN A NEURONAL MODEL OF SYNUCLEINOPATHY

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Introduction: The simultaneous accumulation of different misfolded proteins is a common feature in several neurodegenerative diseases. In most cases, these proteins are found in different brain regions and cell populations, but in some instances the proteins can be found in the same aggregates. Some synucleinopathies show abnormal deposits of both α-synuclein and tau in the same protein aggregates. Although it is known that tau and α-synuclein may have synergistic effects on their fibrillization, the underlying biological effects remain poorly understood.

Aims: To investigate in detail the effects of tau on α-synuclein aggregation in a neuronal model of α-synuclein aggregation.

Methods: Human neuroglioma cells (H4), primary neuronal cultures, transfection, fluorescence resonance energy transfer (FRET).

Results: In this model we observed, by confocal microscopy and FRET-based techniques, that tau colocalizes and interacts with α-synuclein in the aggregates. We also found that tau overexpression increased α-synuclein levels in the insoluble protein fraction, the number of aggregates and the amount of high molecular weight species. Taken together, these data suggest that tau enhances α-synuclein aggregation and may contribute to the deleterious effect of α-synuclein in neurodegenerative diseases that show both pathologies.