Déchiffrer l'agrégation de la protéine tau par RPE continue et impulsionnelle.

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Résumé

The intrinsically disordered tau protein is known to aggregate into amyloid filaments involved in many neurodegenerative diseases, including Alzheimer's disease (AD) and Pick's disease (PiD). Different aggregate structures are involved in distinct pathologies and seems to be able to propagate in a prion-like manner. Yet, the basic mechanism or factor that directs tau aggregation and structural differentiation remains unknown. We combined continuous wave (cw) and pulse electron paramagnetic resonance spectroscopy (EPR) with biochemical techniques to characterize various aspect of tau aggregation. Quantitative analysis of cw-EPR spectra allowed to distinguish oligomeric species and characterize intermediate states of tau aggregation. Using double electron-electron resonance spectroscopy (DEER), we characterized tau structural properties, both in soluble and amyloid states. We showed that recombinant tau filaments, produced in vitro with heparin, are structurally heterogeneous and very different from aggregates found in AD and PiD brains. Furthermore, we showed that the presence of mouse brain-extracted seeds in the aggregation assay selects well-defined structured aggregates, as opposed to heterogeneous filaments formed without seeds.

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