HYPERPHOSPHORYLATION OF TAU PROTEIN HAS A PROTECTIVE ROLE IN PREVENTING NEURONAL DEATH DUE TO THE TOXICITY OF C-TERMINALLY TRUNCATED TAU IN ALZHEIMER'S DISEASE

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The hyperphosphorylation and C-terminal truncation of tau protein have been proposed as key events leading to the assembly of paired helical filaments (PHF) in Alzheimer´s disease (AD). Through the biochemical analysis of PHF it has been possible to identify two subpopulations of such structures: dispersed, sarkosyl-insoluble PHF which are characteristically hyperphosphorylated and protease-resistant PHF that are highly insoluble. The main component of the latter filaments is a fragment of tau protein corresponding to the repeated domain and which is truncated C-terminally at Glu-391. This fragment is the major constituent of the "PHF core" and is recognized by the monoclonal antibody (mAb) 423. In previous studies we have study pretangle cells (pNFT) and demostrated that there is an early and specific cascade of phosphorylation of sites along the N-terminus of tau, as well as conformational changes. In the present study, by examining pNFT, our aim was analyzed the relationship between phosphorylation along the C-terminus of tau and the presence of truncation at the Glu-391 and thiazin red. Were used in double and triple immunolabelling with a variety of tau marker and analyzed by microscopy confocal. We were able to expose mAb 423 in pNFT only after a pre-treatment with Pronase and formic acid. The mAb 423 and S396 immunoreactivities were found colocalized in small tangles but not so in pNFT. These findings are discussed in the controversial context of whether tau oligomers and NFT play either a neuroprotective or neurotoxic role in AD.

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