

FORMALDEHYDE INDUCING AN AMYLOID-LIKE AGGREGATION OF HUMAN NEURONAL TAU

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It was reported that tau, which was isolated from an AD brain, aggregated into globular condensates and extended condensates although tau was demonstrated to form paired helical filaments (PHFs) pathologically (Ruben et al. 1997, *Synapse*, 27:208). Formaldehyde was formed from methanol by human liver microsomal enzymes. This compound can react with biologically active proteins, however, no reports have exhibited whether or not it reacts with human neuronal tau that plays an important role in assembly and stabilization of microtubule. Formaldehyde was found to induce neuronal tau to aggregate in our experiments. The intensity of light scattering of tau solution at 480 nm increased markedly when treated by formaldehyde at low concentrations, with the loss in tau's function. The concentration of the aldehyde that induced a half of tau to aggregate was approx. 0.3%, and it was 0.9% in case of phosphorylated tau catalyzed by neuronal Cdk5 like kinase. A distinguishable decrease in the intrinsic fluorescence of tau occurred in 0.1% formaldehyde solution, indicating a change in its molecular conformation. Under electronic microscope, the formaldehyde treated tau had globe-like spatial structures and protein-clumps in different sizes. No PHFs were observed. It was suggested that formaldehyde at low concentration could induce tau into an amyloid-like deposit.