NOVEL TRANSGENIC RAT MODEL FOR HUMAN TAUOPATHY SHOWS NO NEURONAL LOSS DESPITE OF PROGRESSIVE NEUROFIBRILLARY DEGENERATION IN THE CORTEX

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Neurofibrillary degeneration induced by misfolded protein tau and neuronal loss are considered to be major pathological hallmarks of Alzheimer disease (AD) and related human tauopathies. Both pathological features showed similar spatio-temporal distribution, however the issue whether tau neurodegeneration can induce neuronal death remains open. These findings emphasize the need for rigorous analysis of neurofibrillary lesions induced by expressing human truncated tau with three repeat domains, in novel transgenic rat model. In this work we analyzed transgenic males to clarify impact of modified human truncated tau on central nervous system. Transgenic rats developed progressive age-dependent neurofibrillary degeneration in the rat brain isocortex. Neurofibrillary tangles (NFTs) satisfied several key histological criteria used to identify neurofibrillary degeneration in the human AD including argyrophilia, Congo red birefringence and Thioflavin S reactivity. NFTs were also identified with antibodies used to detect pathologic tau in human brain, including DC11, recognizing an abnormal tau conformation and antibodies that are specific for hyperphosphorylated tau protein. Moreover, transgenic rats developed extensive sarcosyl insoluble tau protein complexes consisting of hyperphosphorylated rat endogenous and truncated tau species. In spite of that, transgenic rats showed neuronal loss neither in the cortex nor in the hippocampus. These results suggest that progressive neurofibrillary degeneration induced by misfolded truncated tau does not cause neuronal loss in the brain of the novel transgenic rat model for human tauopathy.

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