02 - B. Neurofibrillary tangles (NFT)

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1. Alzheimer’s Dementia (AD)

Gross changes include diffuse atrophy, flattened cortical sulci and enlarged cerebral ventricles. Histological changes include neuronal loss (particularly in the cortex and the hippocampus), synaptic loss, granulovascular degeneration (small vacuoles with central granules, in the cytoplasm of neurons especially in the temporal lobes), senile plaques, neurofibrillary tangles and Hirano bodies. Astrocytic gliosis and microglial activation are also noted in some cases. A. Senile plaques Plaques are insoluble amyloid peptide deposits. The peptide involved is called Aß (beta A4) peptide. Amyloids are fibrils of multimeric chains of peptides deposited extracellularly. They have a beta pleated sheet confirmation. Aß is cleaved from a larger transmembrane protein—amyloid-ß precursor protein—by the action of ßand -secretases and its formation is prevented by the action of -secretase. Plaques vary in appearance, and two main subtypes are recognised. Neuritic plaques: o They contain Aß in the form of amyloid fibrils, among which are irregularly swollen dystrophic neurites (degenerated neuronal processes). o The neurites are well visualised with silver stains; they may be seen as an eosinophilic mass on haematoxylin & eosin stains. o Neuritic plaques may contain a dense central core of amyloid. o Microglia and astrocyte processes are present towards the periphery of neuritic plaques. o Seen in Down syndrome and, to some extent, in normal aging as well. o Amyloid sensitive stain Congo red, under polarized light, demonstrates the "apple green" birefringence of the stained tissue with neuritic plaques, due to the presence of beta-pleated sheets. Diffuse plaques: o They consist largely of non-fibrillar extracellular Aß. o They are not related to the degree of cognitive decline o Diffuse plaques contain the same peptides as those responsible for amyloid formation in the neuritic plaques. However, these peptides are not polymerized to form fibrils and lack beta-sheet configuration o Only neuritic plaques are counted in neuropathological tests. B. Neurofibrillary tangles (NFT) NFT are composed of cytoskeletal elements, primarily abnormally phosphorylated tau protein. AD is one of the several degenerative tauopathies. Tau is a peptide required for microtubule assembly. Microtubules are essential to transport of materials down the axons.

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