The biological basis for the selective vulnerability of neurons in Alzheimer's disease (AD) is elusive. Aggrecan-based perineuronal nets (PNs) of the extracellular matrix have been considered to contribute to neuroprotection in the cerebral cortex. In the present study, we investigated the organization of the aggrecan-based extracellular matrix in subcortical regions known to be predominantly affected by tau pathology in AD. Immunocytochemistry of aggrecan core protein was combined with detection of neuronal markers and hyperphosphorylated and aggregated tau indicating neurofibrillary tangles and neuropil threads. The results showed that many regions showing severe tau pathology in AD were devoid of a characteristic aggrecan-based extracellular matrix. Regions composed of nuclei with clearly different intensity of tau pathology, such as the amygdala, the thalamus and the oculomotor complex, showed largely complementary distribution patterns of neurofibrillary tangles and PNs. Quantification in the reticular interstitial nucleus of the longitudinal fascicle potentially affected by tau pathology in AD revealed that tau pathology was not accompanied by loss of aggrecan-based PNs. Fibrillary tangles in net-associated neurons extremely rarely occurred in the pontine reticular formation. Distinct tau pathology was observed in the subthalamic nucleus in neurons devoid of PNs but contacted by fibers associated with axonal coats of aggrecan-based extracellular matrix. We conclude that the low vulnerability of neurons ensheathed by PNs previously described for cortical areas in AD also exists in subcortical regions. The aggrecan-based extracellular matrix of PNs may be involved in neuroprotection.