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Hippocampal distribution of tau pathology in FTLD tauopathies

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State of the art: The distribution and maturation of tau tangles with conformation-specific markers within the anatomic framework of hippocampal connectivity has been well characterized in Alzheimer's disease (AD). However, there is limited data on the regional patterns and conformations of tau pathology across hippocampal subfields in frontotemporal lobar degeneration tauopathies (FTLD-tau).

Methodology: Patients with neuropathological diagnoses of Pick's disease (PiD,N=11), corticobasal degeneration (CBD,N=23), and progressive supranuclear palsy (PSP,N=52) with none-to-low levels of AD co-pathology; clinically-similar non-amnestic variants of AD (N=39) were included as a reference group. Digital histology methods measured percent area occupied in hippocampal subfields using tau immunolabelled for phosphorylated-tau (AT8) and C-terminally truncated tau (MN423), which labels mature tangles in AD. Linear mixed-effect models tested regional differences compared to dentate gyrus (DG) in each group while adjusting for demographics.

Results: In PiD, AT8-immunoreactivity was greatest in DG and Subiculum (β=1.6,$p<0.001$) with low levels of MN423 reactivity in Pick bodies in DG, CA1, Subiculum and entorhinal cortex (ERC). In CBD, AT8-immunoreactivity was highest in CA1 (β=1.2,$p<0.001$), CA2 (β=0.8,$p<0.001$), and subiculum (β=0.8,$p<0.001$). PSP AT8-immunoreactivity was largely focused in CA2 (β=0.8,$p<0.001$) and ERC (β=0.8,$p<0.001$), and less severely in CA1 (β=0.4,$p<0.001$) and Subiculum (β=0.4,$p<0.001$). MN423 reactivity was largely absent in CBD and PSP. In comparison, AD showed greatest burden of AT8 and MN423-immunoreactivity in CA1, CA2, Subiculum and ERC ($p<0.001$).

Conclusion: Distinct forms of FTLD tauopathy may have divergent microscopic patterns of spread and posttranslational processing of tau in the hippocampus that diverge from AD tau and traditional AD Braak staging.

Conflicts of interest

I have no conflict of interest.