

Hippocampal vulnerability in Progressive Supranuclear Palsy with Alzheimer's disease co-pathology

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State of the art: Progressive supranuclear palsy (PSP) is a 4-repeat tauopathy that can present with Alzheimer's disease (AD) co-pathology. The goal of this study is to investigate whether subcortical vulnerability is associated with AD pathology in PSP.

Methodology: 53 PSP patients and 8 controls underwent structural and functional magnetic resonance imaging (MRI). Patients were divided into AD biomarker positive (10 PSP-AD) and negative (43 PSP-noAD) based on AD biomarkers in cerebrospinal fluid, blood or amyloid PET. Subcortical volumes (brainstem, basal ganglia, thalamus, amygdala and hippocampus) were obtained by Freesurfer segmentation, corrected for total intracranial volume and then compared between groups using ANOVAs. Functional MRIs were preprocessed using the CONN toolbox. Subcortical networks based on each of the structural regions were investigated between PSP-noAD and PSP-AD by two-sample *t*-tests. All analyses were corrected by age and scanner.

Results: Both PSP-AD and PSP-noAD displayed brainstem atrophy and PSP-noAD, of the left thalamus in comparison to controls (all post-hoc $p < 0.05$). PSP-AD had smaller left hippocampal volume versus controls (post-hoc $p = 0.02$) and PSP-noAD (post-hoc $p = 0.08$). PSP-AD had less connectivity between the left hippocampus, the posterior cingulate cortex, the precuneus and the right temporal lobe ($p < 0.001$, FDR cluster correction); and between the right hippocampus and the left frontal pole ($p < 0.001$) in comparison to PSP-noAD.

Conclusion: Hippocampal vulnerability was observed in PSP-AD compared with PSP-noAD, suggesting that the hippocampus is vulnerable to AD co-pathology. These results highlight the need for biomarkers to disentangle the heterogeneity in PSP.

Conflicts of interest

N/A