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Friday

Neuronal loss of the nucleus basalis of Meynert in primary progressive aphasia is associated with Alzheimer's disease neuropathological changes

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State of the art: Clinical imaging studies indicated basal forebrain reduction in primary progressive aphasia (PPA), which might be a candidate marker for cholinergic treatment. Neuronal loss in the nucleus basalis of Meynert (nbM) has been reported, but a systematic quantitative assessment including the three clinical variants of PPA is lacking.
Methodology: Quantitative assessment of neuronal density and pathology was performed on nbM tissue of 47 cases: 15 PPA, belonging to the different clinicopathological phenotypes, 14 Alzheimer's disease (AD) and 18 cognitively normals. Immuno-labelled sections (AT8: ptau and pTDP-43) were microscopically analyzed using ImageJ. Kruskal-Wallis analysis of variance with post hoc Bonferroni corrected Dunn tests was applied to assess neuronal density across groups. Additionally, single case t-statistics for each patient were calculated using Matlab R2014b. Spearman correlation assessed which pathological variables correlated with nbM neuronal density and these variables were subsequently entered into k-fold cross-validated support-vector machine (SVM) regressions (R package caret) and in a multi-model inference analysis (R package MuMIn).
Results: Group-wise, reduced nbM neuronal density was restricted to AD patients ($pcorr.$=0.0487). At the individual patient level, semantic variant PPA with underlying AD neuropathological change had lower neuronal densities, while neuronal density was unaffected in those with TDP-43 type C. SVM indicated that nbM neuronal loss was associated with higher Braak neurofibrillary tangle stage (p<0.001) and increased numbers of nbM-related pretangles (p=0.017).
Conclusion: nbM neuronal loss in PPA is related to AD neuropathological changes. This study cautions against overinterpreting MRI-based basal forebrain volumes in non-AD PPA as neuronal loss.

Conflicts of interest

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