

## Trajectories of neurocognitive decline in aphasic versus behavioral dementia syndromes due to Pick disease

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**State of the art:** This study compared rates of neurocognitive decline and pathologic burden in two distinct dementia syndromes—primary progressive aphasia (PPA) and behavioral variant frontotemporal dementia (bvFTD)—caused by FTLD 3R-tauopathy of Pick disease (PiD).

**Methodology:** Eleven cases with postmortem PiD were identified from the Northwestern ADRC brain bank (bvFTD, N=6; PPA, N=5). Uniform composite scores for global cognition, language, executive function, and memory were calculated from yearly visits. Domain-specific rates of decline (i.e., slope) were calculated between initial visit (1-5 years from symptom onset; global CDR=0.5-1) and final visit (1-year prior to ‘untestability’ due to disease severity). Unbiased stereology was performed using AT-8-stained sections from bilateral neocortex [middle frontal, inferior parietal, and superior temporal gyri] per case to quantify Pick body densities. T-tests compared trajectories of decline and pathologic burden between groups.

**Results:** The bvFTD group showed fastest rates of decline (i.e., steepest slope) in global cognition and executive functioning, whereas PPA cases showed fastest decline in language. As expected, executive functioning declined significantly faster in bvFTD than PPA ( $p=0.027$ ). bvFTD patients were rendered “untestable” significantly sooner than PPA patients ( $p<0.05$ ). Stereological analysis revealed significantly greater bilateral neocortical densities of Pick bodies in bvFTD compared to PPA at autopsy ( $p<0.01$ ).

**Conclusion:** Preliminary analysis of domain-specific longitudinal performance appears to be concordant with the behavioral versus aphasic phenotype characteristic of bvFTD and PPA, respectively. Compared to PPA, cases with bvFTD demonstrated faster rates of global and executive decline, likely linked to a relative abundance of PiD in neocortex.

### Conflicts of interest

The authors have no duality or conflicts of interest to declare.