

Overview of a large single-site familial FTD cohort

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BACKGROUND

Frontotemporal dementia (FTD) is a rare disease with an approximate prevalence of 9.17 per 100,000 people¹; approximately 20-25% of cases appear to be familial with a substantial proportion of those being inherited in an autosomal dominant manner.

Diagnosis and prognostication in FTD are challenging due to considerable heterogeneity in clinical presentation and disease progression, and reliable tools remain limited^{2,3}.

Comprehensive longitudinal data capturing clinical features and outcomes are critical for characterizing disease trajectories and identifying factors that may improve diagnostic and prognostic accuracy.

Our program has been recruiting research participants with familial FTD (fFTD) for nearly 20 years into a study focusing on fFTD for people living with a diagnosis and their unaffected family members.

Aim: To describe the characteristics of participants in our fFTD cohort and the available data.

METHOD

Participants are followed annually with comprehensive behavioral neurologic assessments, neuropsychological assessments, structural and functional brain MRI scans, and blood draws.

Some participants undergo skin biopsy for fibroblast sample collection, and some undergo PET scans (FDG, amyloid, and/or tau PET).

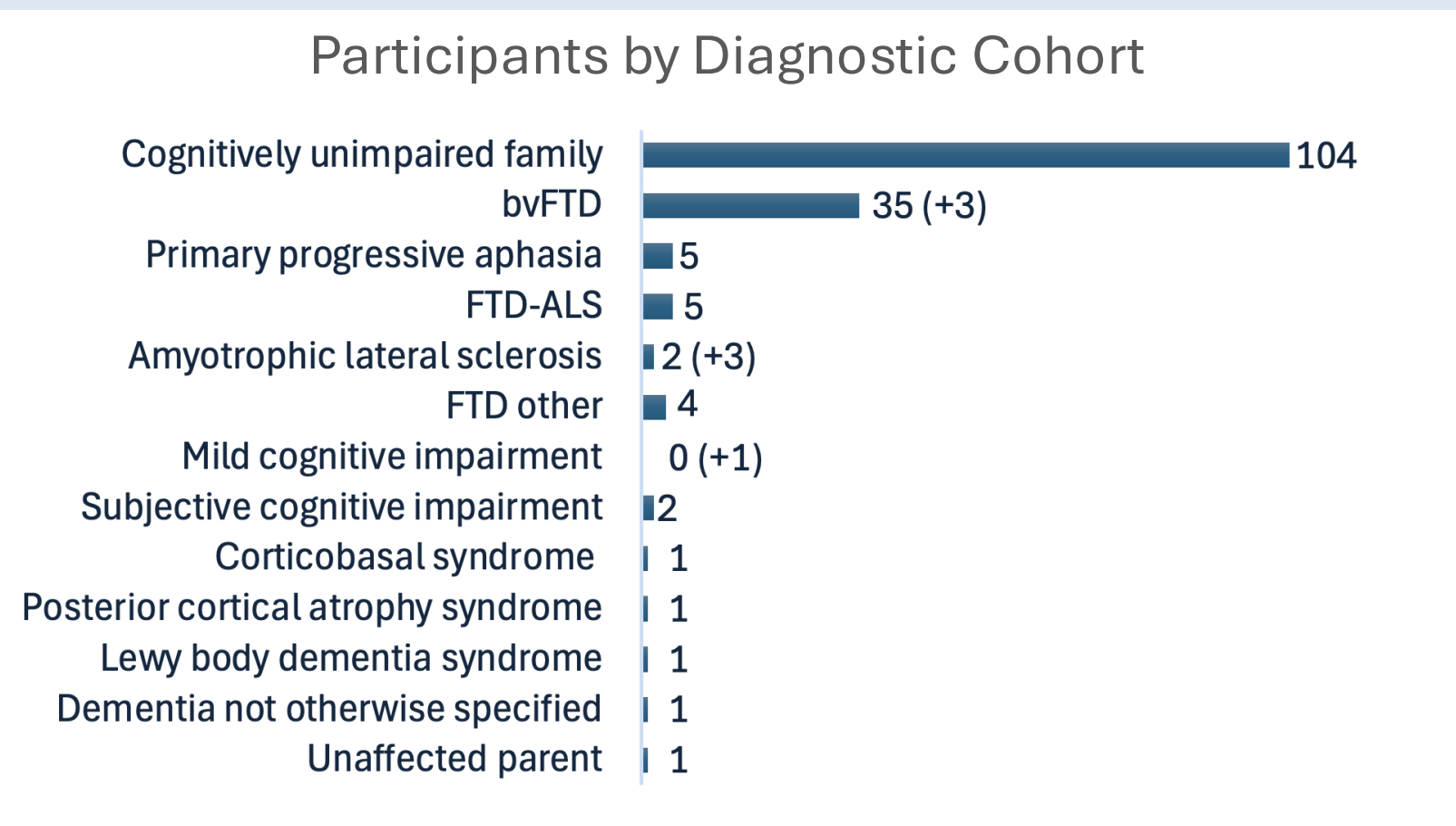
All participants are asked if they would consider post-mortem brain donation. All participants are offered genetic counseling and clinical testing if desired and feedback about interpretable results from visits.

RESULTS

The cohort comprises 163 individuals (83F/80M) across 88 families (mean = 1.79; range 1-10 participating members per family). Mean age was 50.6 ± 13.8 years at baseline and 54.5 ± 14.2 years at most recent visit.

Families carry pathogenic variants in *c9orf72* (55%,n=48), *MAPT* (16%,n=14), *GRN* (16%,n=14), and *ANXA11*, *TARDBP*, or *TBK1* (n=1 each); 8 families have likely autosomal dominant FTLT with no identified mutation.

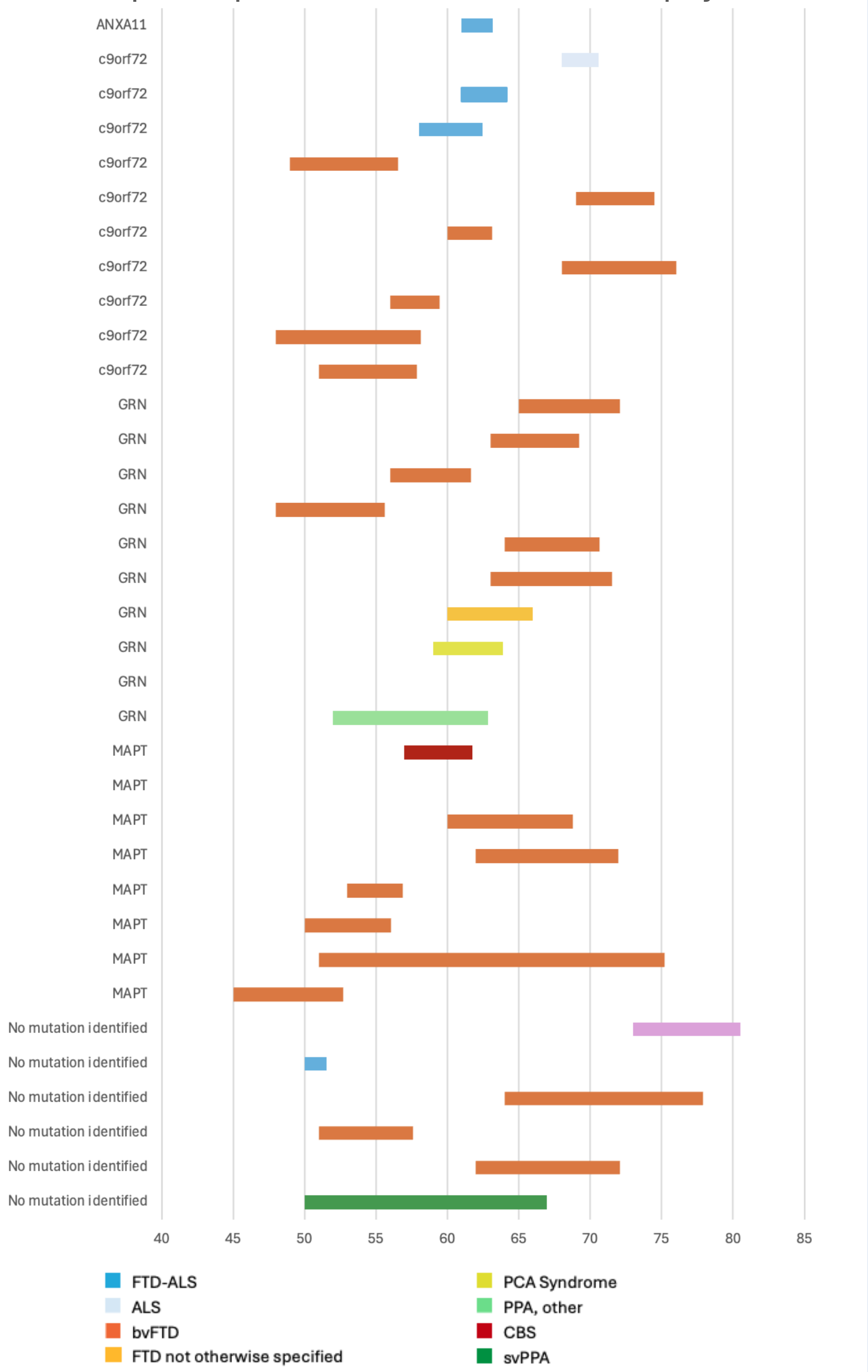
RESULTS, CONT.



Symptomatic participants (n=62) have an average age of onset of 57.62 ± 8.03 (range=37-75). Parenthesis () indicate phenoconversion of fFTD family members who later converted to symptomatic states.

Imaging		
MRI		
Total		401
Participants with at least 1 scan		140
Participants with at least 2 scans		97
Mean scans/person		2.66
Range		1-11
FDG PET		
Total		9
Participants with at least 1 scan		6
Tau PET		
Total		13
Participants with at least 1 scan		13
Amyloid PET		
Total		13
Participants with at least 1 scan		13

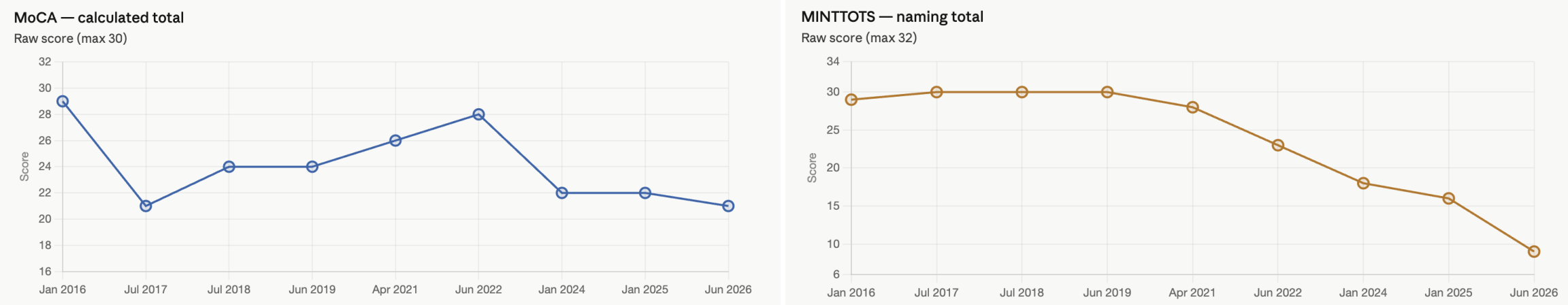
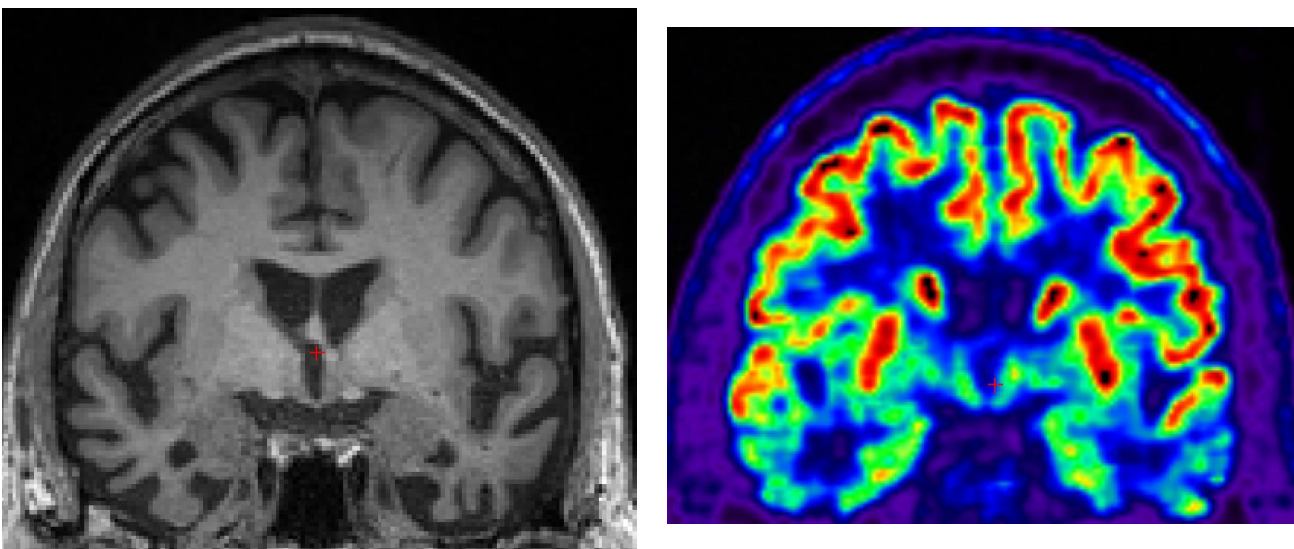
Disease progression (age of onset to age at death) of participants who underwent autopsy



Thirty-five participants underwent autopsies with average age of symptom onset 57.79 ± 7.15 years, average age at death of 65.30 ± 7.46 years, and average time of disease progression 7.35 ± 4.46 years.

CASE SPOTLIGHT

One *MAPT* M+ participant in their early 50s has completed 11 study visits over 14 years of longitudinal follow-up, including neuropsychological exams, 11 structural MRIs, and one each amyloid, tau, and FDG PET, with serial assessments showing a transition from cognitively unimpaired status to an early prodromal symptomatic stage at the most recent timepoint. Daily function is still preserved with minimal evidence of any symptoms or signs in a comprehensive behavioral neurologic examination, and on most tests performance is largely maintained but confrontation naming abilities have declined substantially. MRI and FDG PET show clear evidence of emerging anterior temporal lobe neurodegeneration. This participant consistently said they “wanted to know” any relevant information we are learning from these research visits, so we informed them of these findings. Early identification afforded this participant additional time to engage in personally meaningful activities prior to greater impairment.



CONCLUSION

We continue to follow this well-characterized cohort with the ultimate goals of developing better diagnostic and prognostic markers across pre-symptomatic and symptomatic stages, refining outcome measures, and advancing therapies to slow progression and treat symptoms of fFTD.

REFERENCES & ACKNOWLEDGMENTS

¹Urso et al. (2025). JAMA Neurol.; ²Aderl-Straub et al. (2021). Alzheimer's Dement.; ³Rogalski et al. (2009). Curr Alzheimer Res.

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