

Translational Neuropathology in Neurodegenerative Disease Research



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Postmortem study for biomarker validation and discovery

Tissue-Guided Biomarker Validation and Discovery

Prospective Natural History Studies
Clinical, Genetics, Biofluid, Neuroimaging

**Clinical
Syndrome**

Autopsy

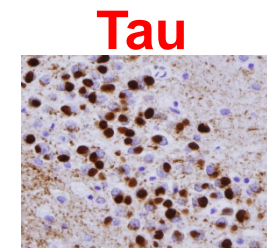
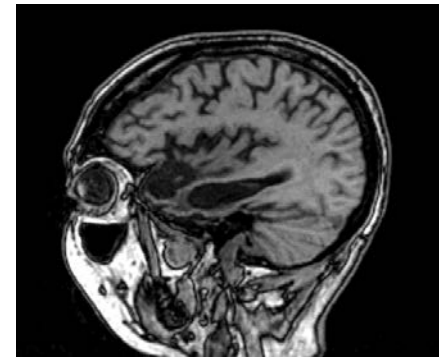
Clinical DNA CSF IMAGING



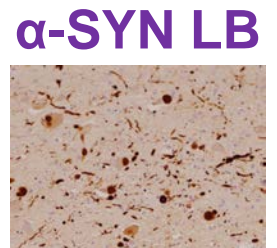
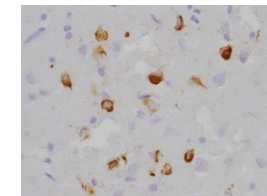
Penn Memory Center
A National Institute on Aging-designated
Alzheimer's Disease Center



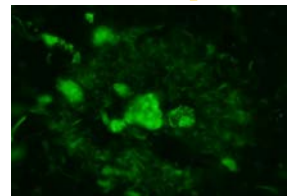
DLBC
Dementia with Lewy
Bodies Consortium



TDP-43

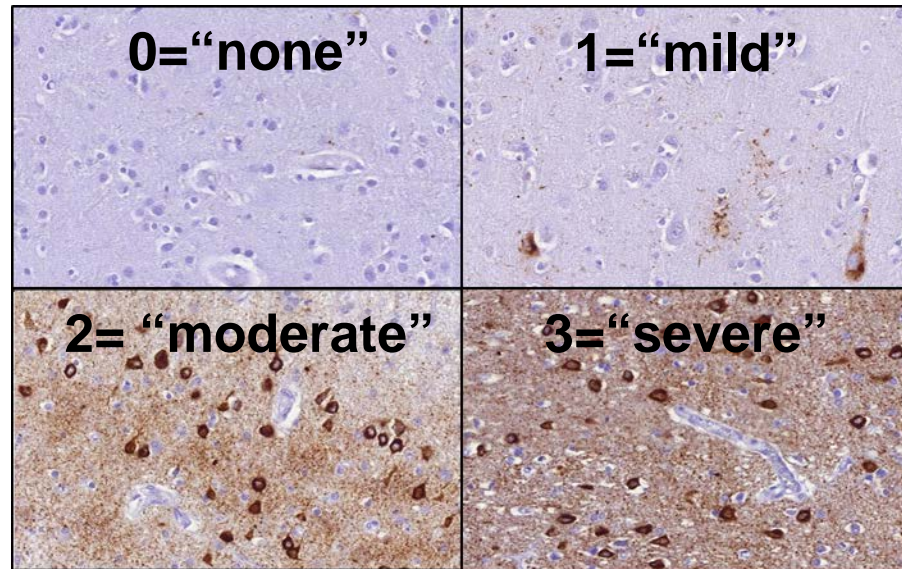


Aβ Plaques



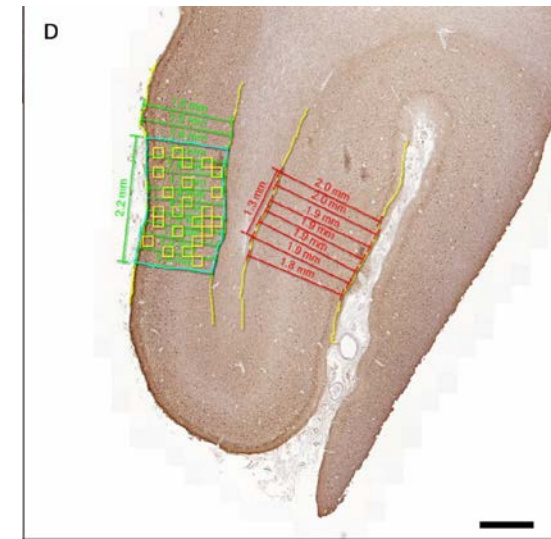
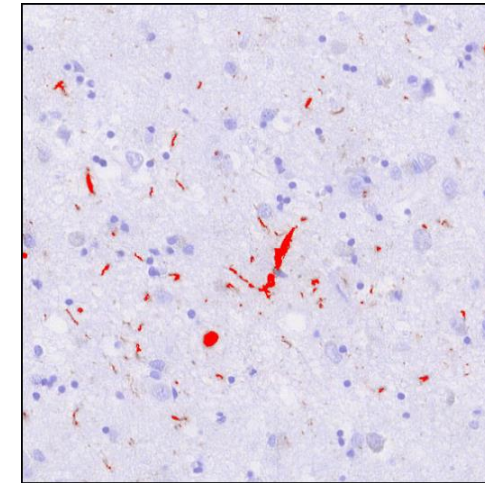
Novel quantitative assessments of pathology

Traditional Scoring



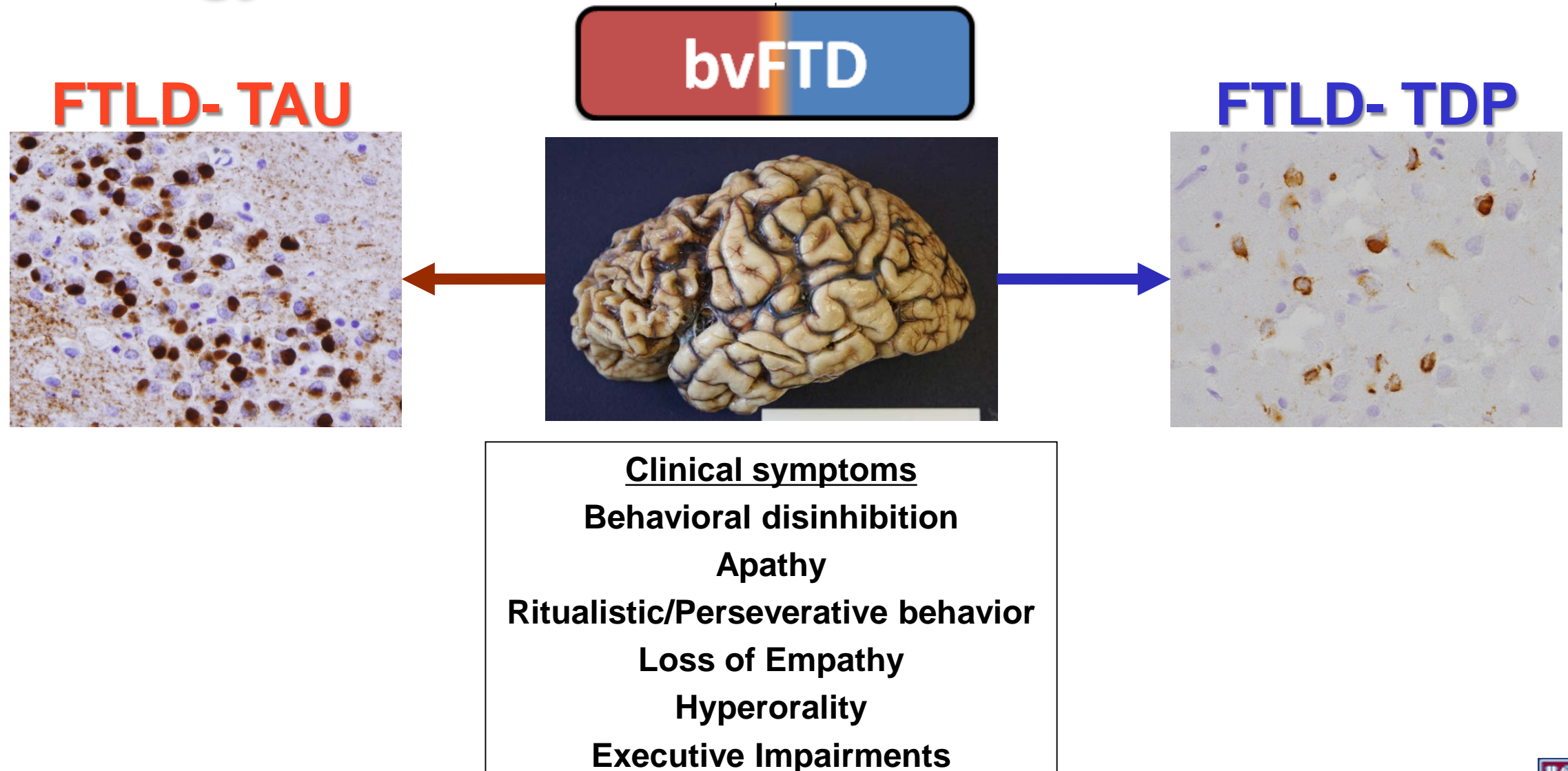
- ◆ Reproducible between labs
- ◆ Subjective, Descriptive > Quantitative

Digital Measurement

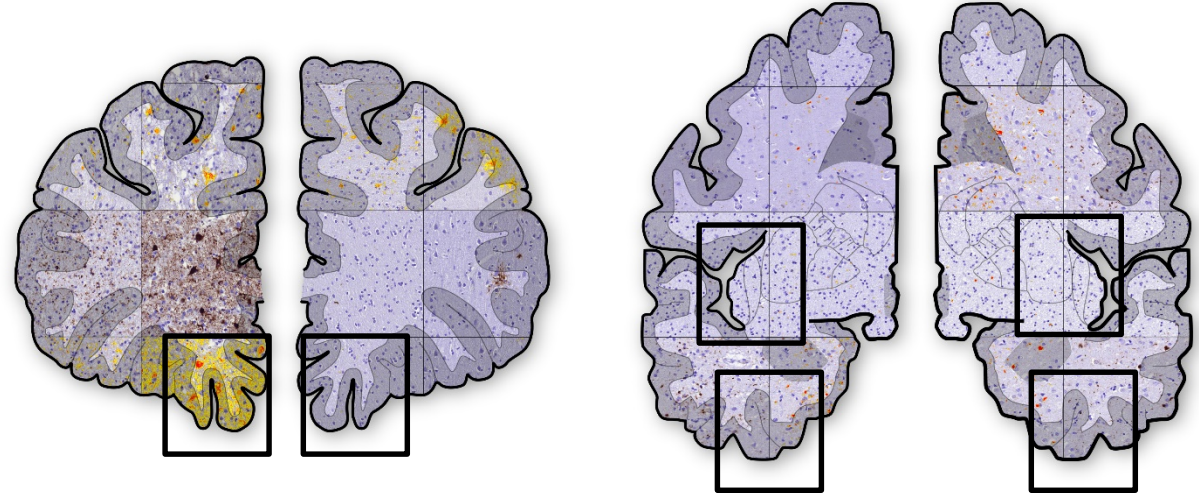
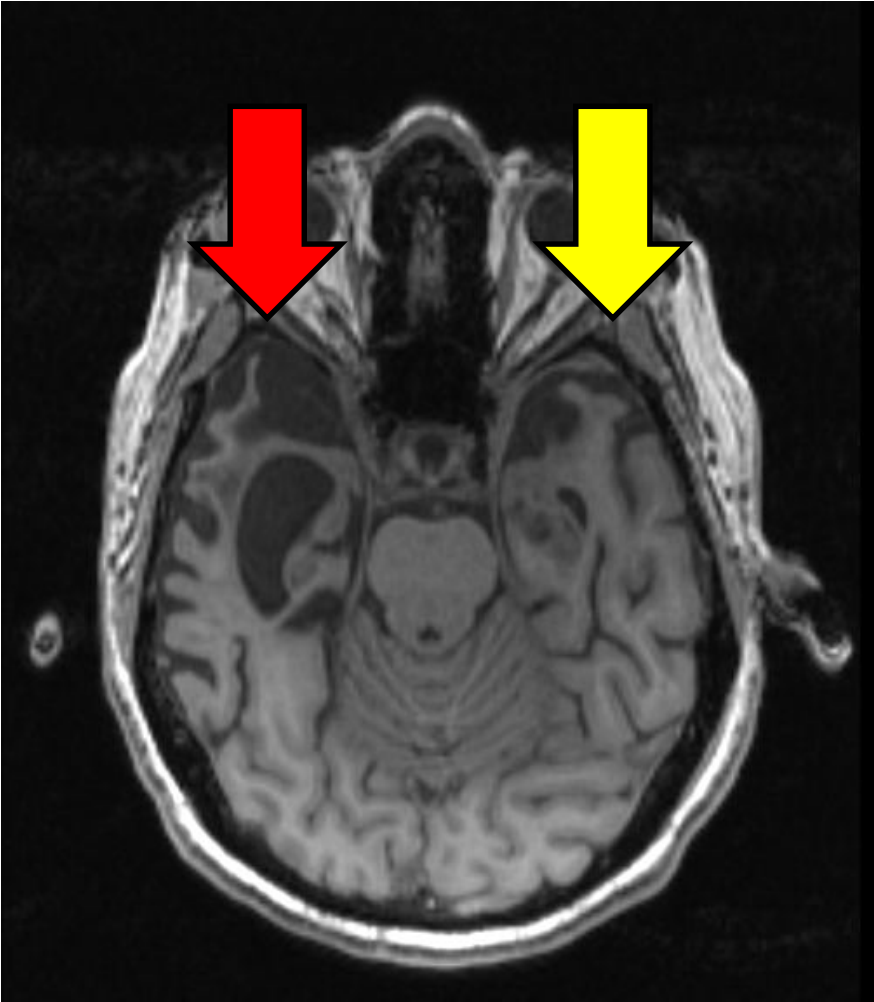


- ◆ Objective
- ◆ Fine-grained data
- ◆ High-throughput
- ◆ Reproducible between labs

Improving antemortem diagnosis of molecular pathology in bvFTD



Asymmetry of FTLD pathology in bvFTD



23 bvFTD bilateral sampling of Insula (INS), Orbitofrontal (OFC), Ventral Temporal (VLT) and Superior Parietal (SPL) Cortex

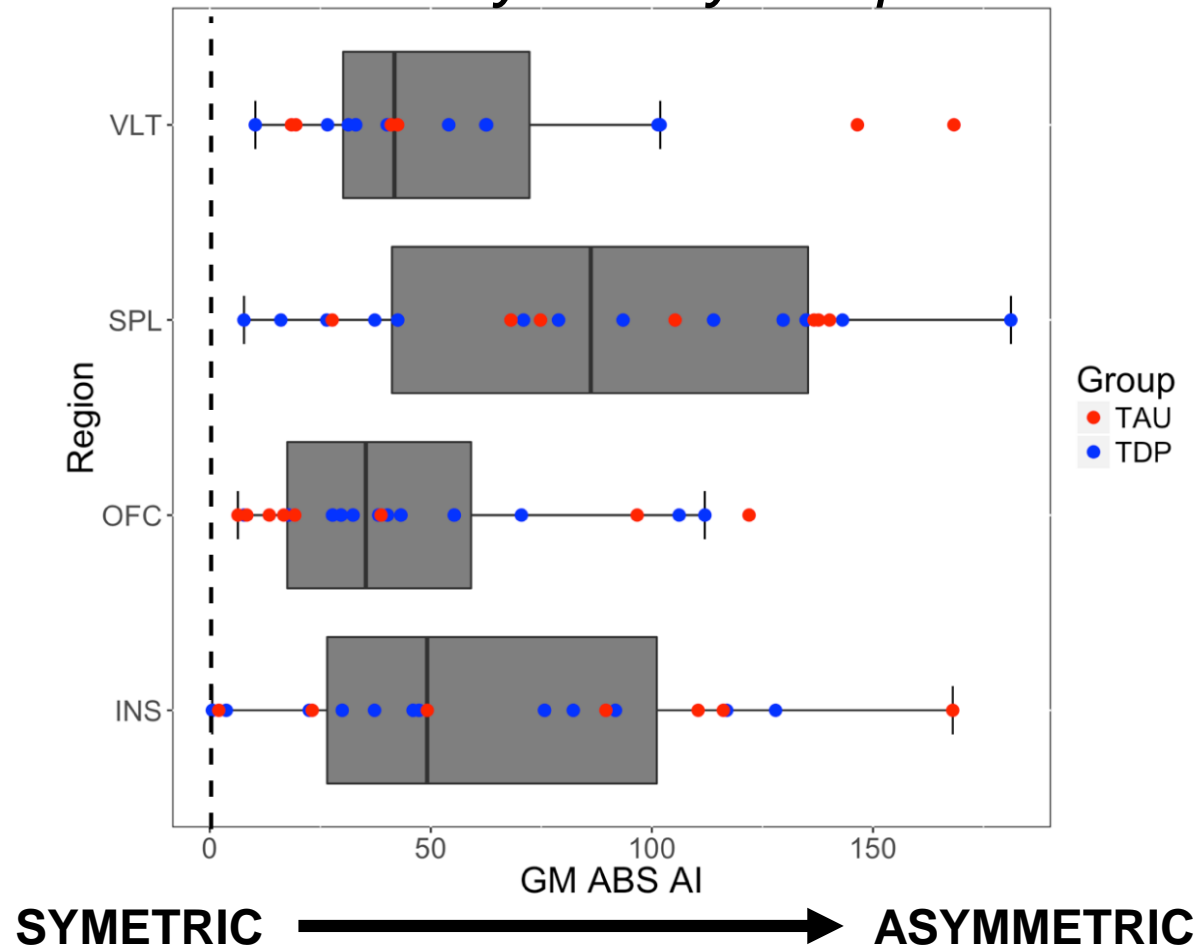
FTLD-TDP = 14

FTLD-Tau = 9

Asymmetry of pathology in bvFTD

$$\text{Asymmetry Index (AI)} = [(R - L) / (\text{Average } R+L)] * 100$$

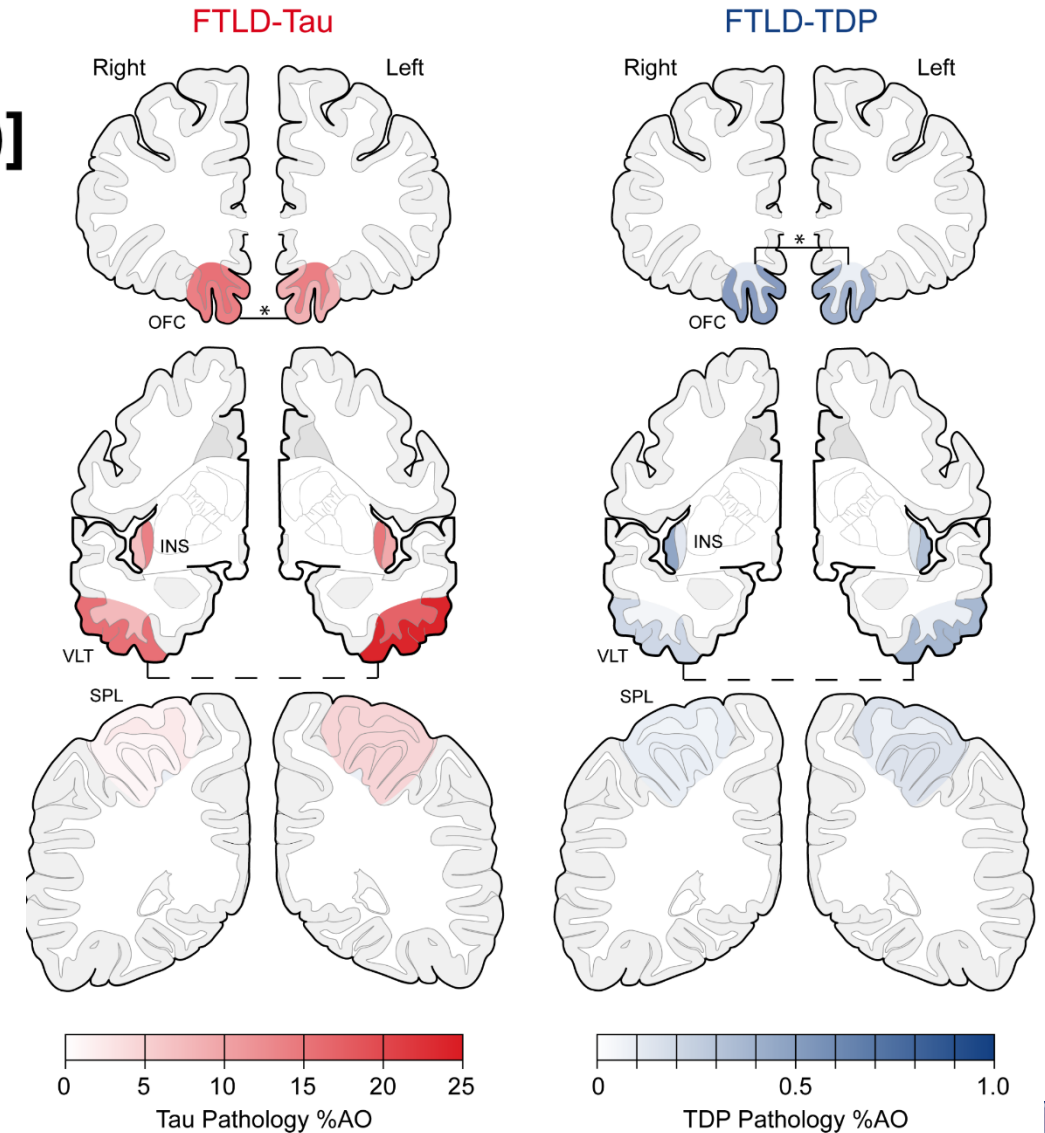
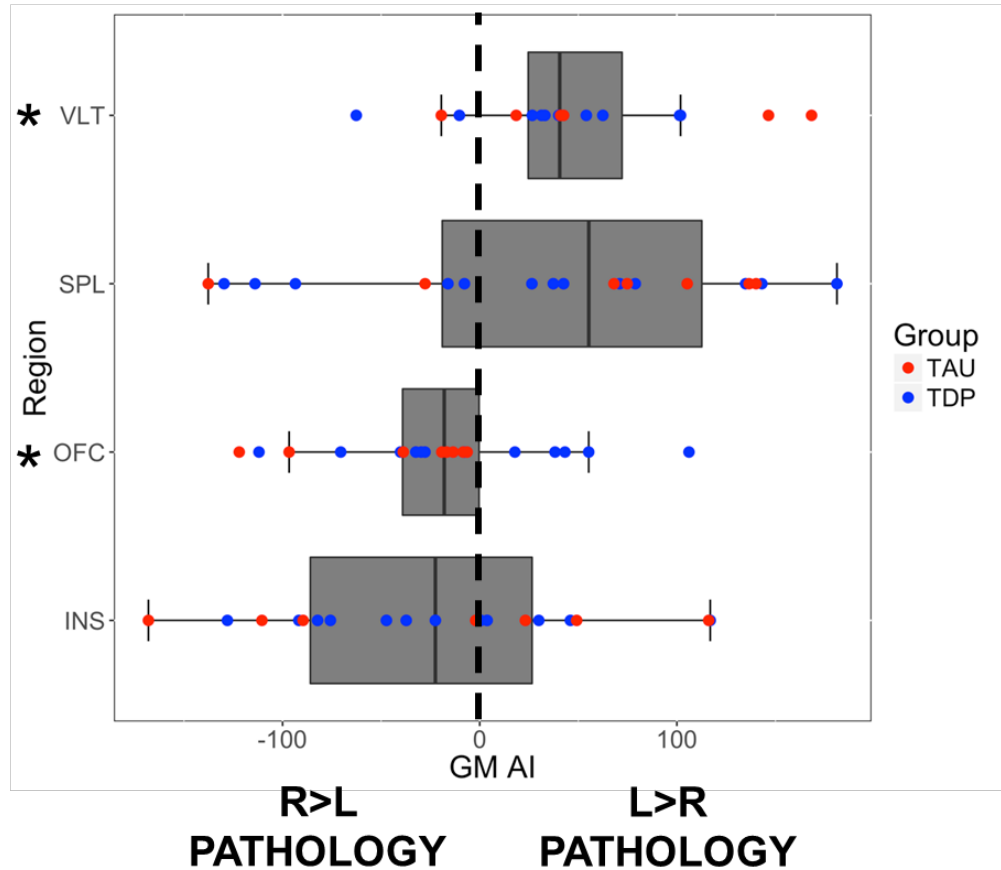
Absolute value of AI = asymmetry independent of direction



One sample t-test for
 $H_0=0$ $p<0.001$ all

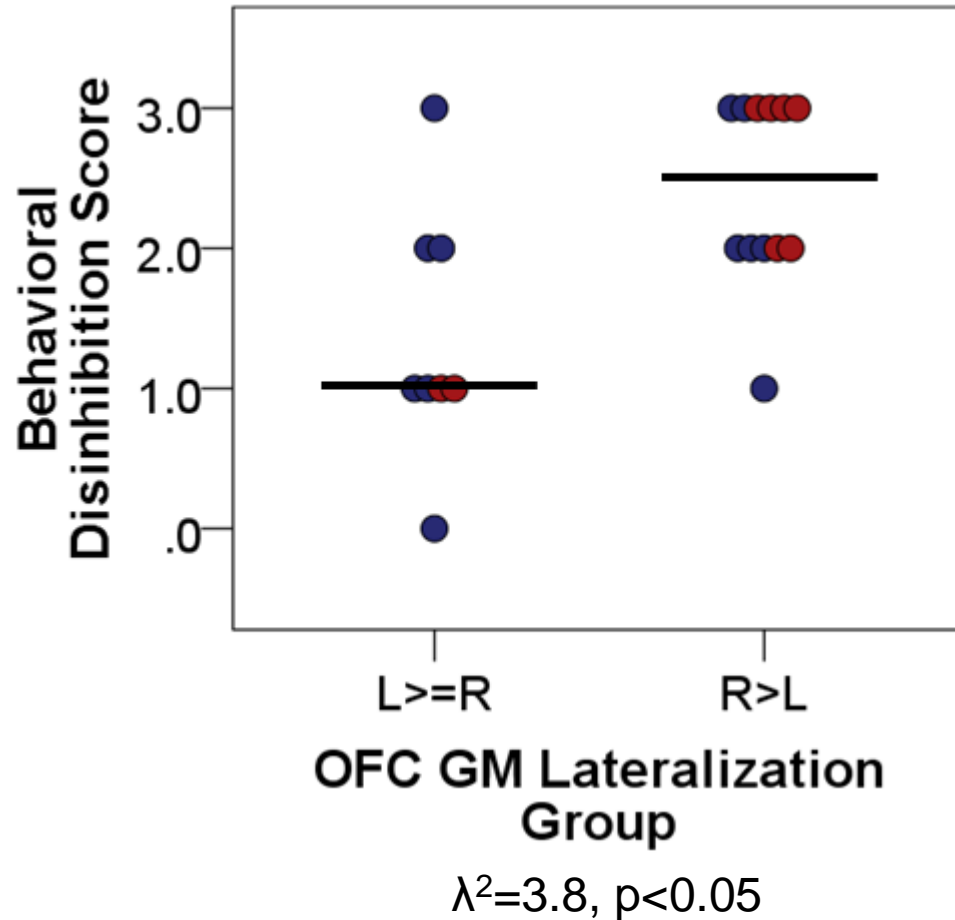
Asymmetry of pathology in bvFTD

Asymmetry Index (AI) = $[(R - L) / (\text{Average } R + L)]$

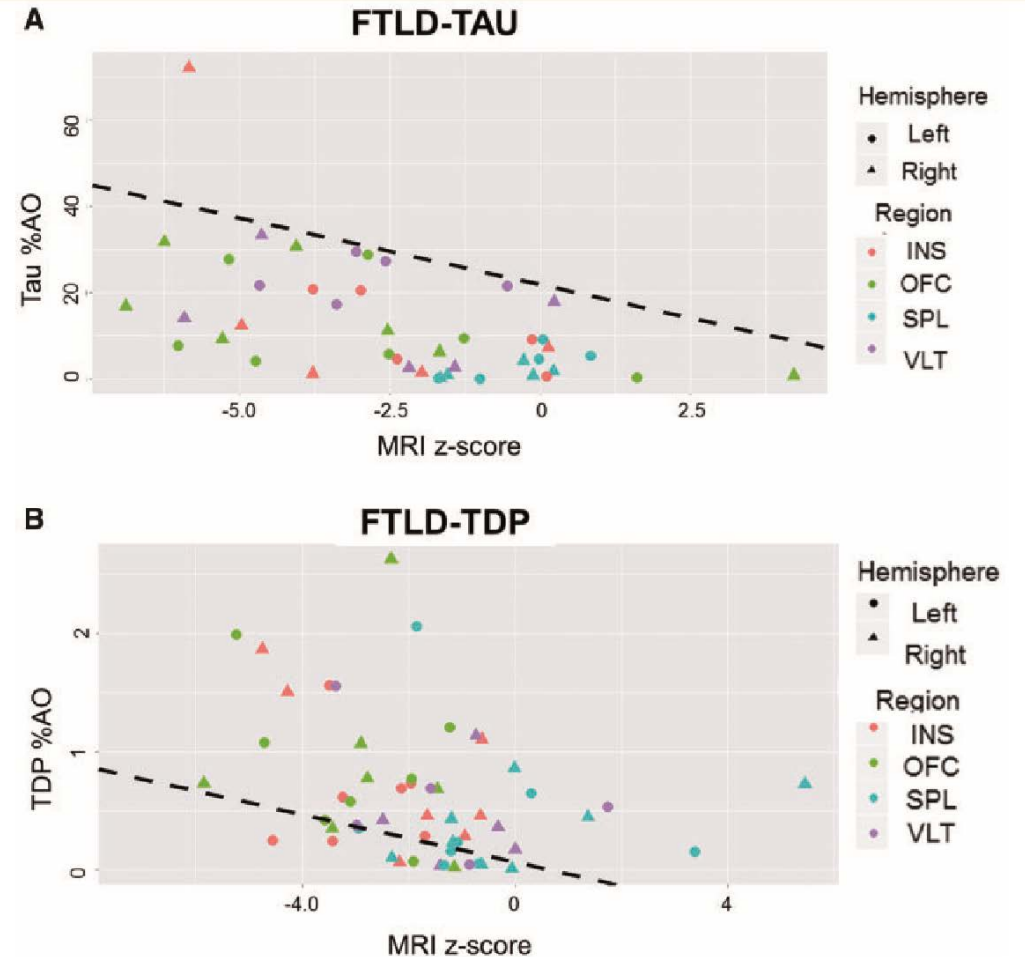


Asymmetry of pathology in bvFTD

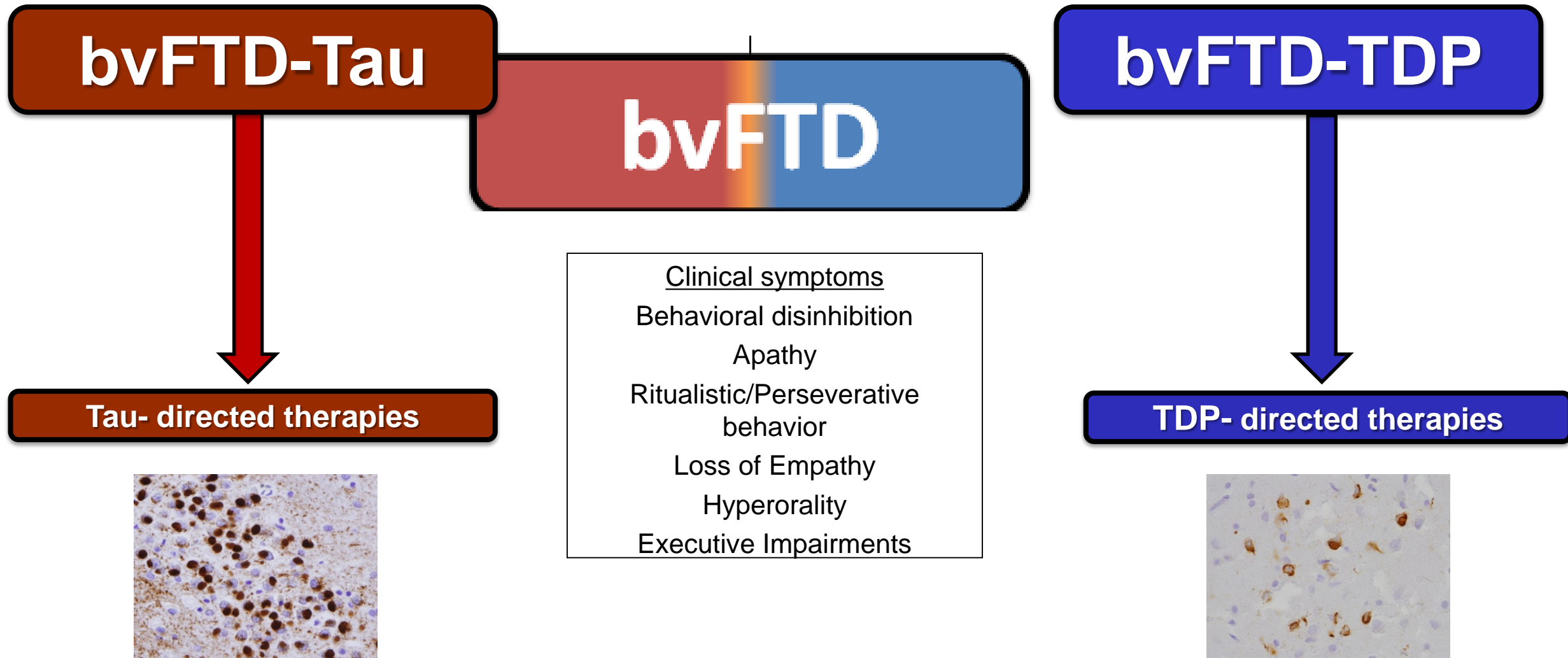
CLINICAL DATA



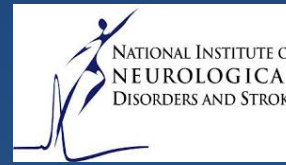
MRI DATA



The goal of bvFTD diagnosis: FTLD-Tau vs FTLD-TDP



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National Institute
on Aging



Patients and their families

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