

# Mobile Cognitive Assessment is Associated with Frontotemporal Integrity and Enhances Disease Classification Beyond Imaging

Ashley Heywood<sup>1</sup>, Amy Wolf<sup>1</sup>, Yann Cobigo<sup>1</sup>, Emily W. Paolillo<sup>1</sup>, Mark Sanderson-Cimino<sup>1</sup>, Jack C. Taylor<sup>1</sup>, Hilary W. Heuer<sup>1</sup>, Sreya Dhanam<sup>1</sup>, Joshua Downer<sup>1</sup>, Ray Fregly<sup>1</sup>, Kaitlin Casaletto<sup>1</sup>, Joel H. Kramer<sup>1</sup>, John Kornak, Leah K. Forsberg<sup>2</sup>, Bradley F. Boeve<sup>2</sup>, Adam L. Boxer<sup>1</sup>, Howard J. Rosen<sup>1</sup>, & Adam M. Staffaroni<sup>1</sup>, on behalf of the ALLFTD Consortium

<sup>1</sup> Department of Neurology, Fein Memory and Aging Center, Weill Institute for Neurosciences, University of California, San Francisco, CA, USA

<sup>2</sup> Epidemiology & Biostatistics, University of California, San Francisco, CA, USA

<sup>3</sup> Department of Radiology, Mayo Clinic, Rochester, MN, USA



UCSF Weill Institute for Neurosciences  
Fein Memory and Aging Center

## Background

- Mobile cognitive assessments offer a reliable, valid, scalable paradigm for capturing sensitive brain health measures<sup>1-3</sup>
- The relationship between remotely delivered cognitive assessments and white matter structural integrity has not yet been explored
- The additive value for diagnostic classification accuracy has not been previously determined

## Methods

- Eighty-nine participants were recruited from the UCSF Fein Memory and Aging Center (Table 1)
- Participants completed cognitive assessments remotely via the ALLFTD mApp and a composite score (SmrtFactor3) was derived:
  - Stroop
  - Flanker
  - Card sorting
  - N-Back
  - Go-NoGo
  - Associative Memory
- T1-weighted images were used to calculate volume across 5 bilateral lobes
- DWI images were processed to calculate fractional anisotropy (FA) and mean diffusivity (MD) across 18 bilateral fiber tracts
- Tracts were averaged into frontal, temporal, and posterior composite measures
- Linear regression models mApp cognitive performance relationships with imaging
- Logistic regression models predicted FTLDCDR Global score impairment using imaging and mApp performance to calculate AUC

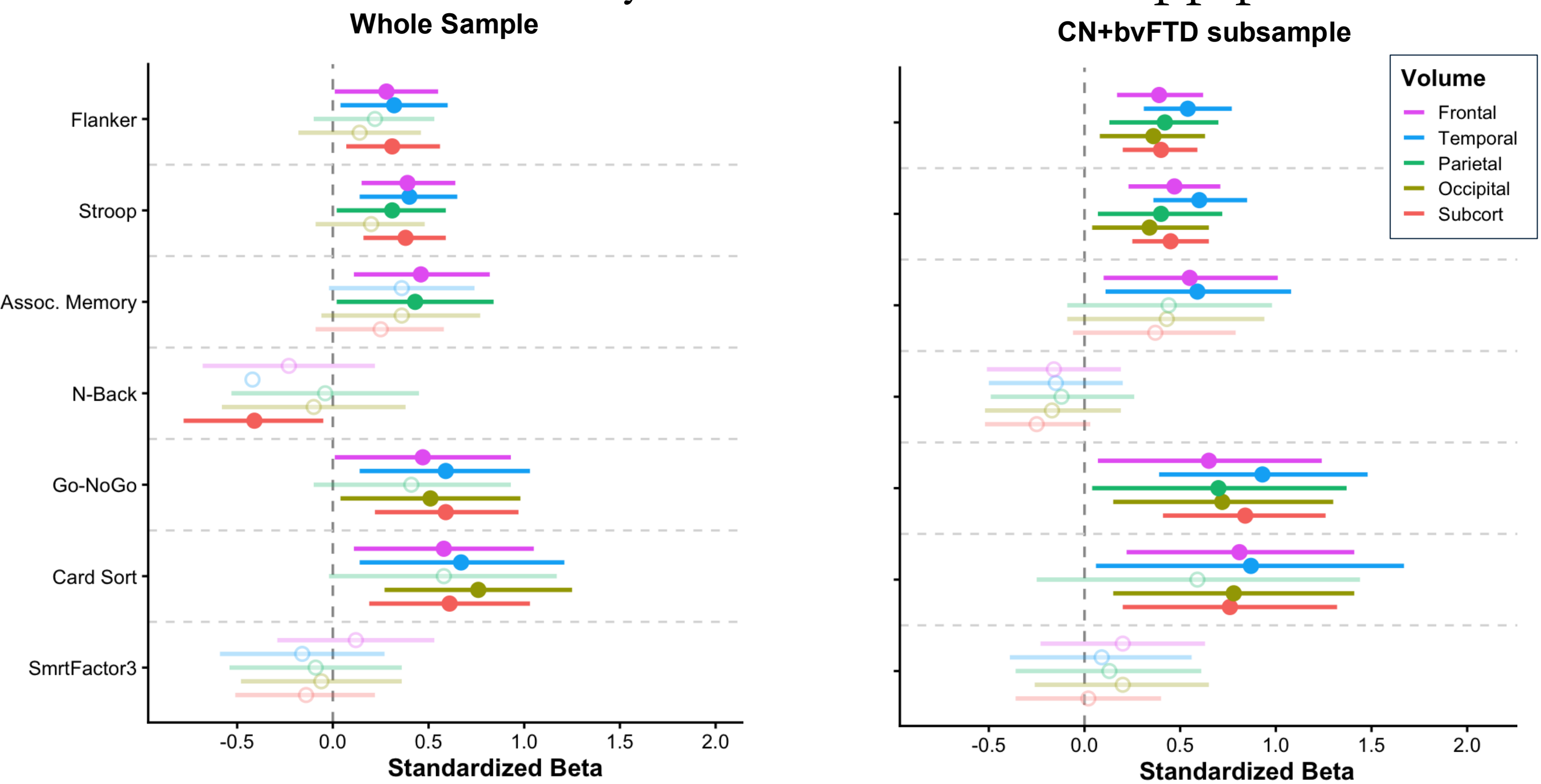
Table 1 – Sample Characteristics

|                          |             |
|--------------------------|-------------|
| N                        | 89          |
| Age M (SD)               | 58.8 (15.5) |
| Sex – female n (%)       | 45 (50.6%)  |
| Education M (SD)         | 16.9 (2.3)  |
| Clinical Diagnosis       |             |
| Clinically Normal n (%)  | 37 (41.5%)  |
| MCI n (%)                | 9 (9.0%)    |
| FTLD syndrome n (%)      | 35 (39.3)   |
| Other n (%)              | 8 (8.9%)    |
| mApp task completion     |             |
| Flanker n (%)            | 81 (91.0%)  |
| Stroop n (%)             | 80 (89.9%)  |
| Associative Memory n (%) | 56 (62.9%)  |
| N-Back n (%)             | 50 (56.2%)  |
| Go-NoGo n (%)            | 46 (51.7%)  |
| Card Sort n (%)          | 38 (42.7%)  |
| Smrt Factor n (%)        | 39 (43.8%)  |

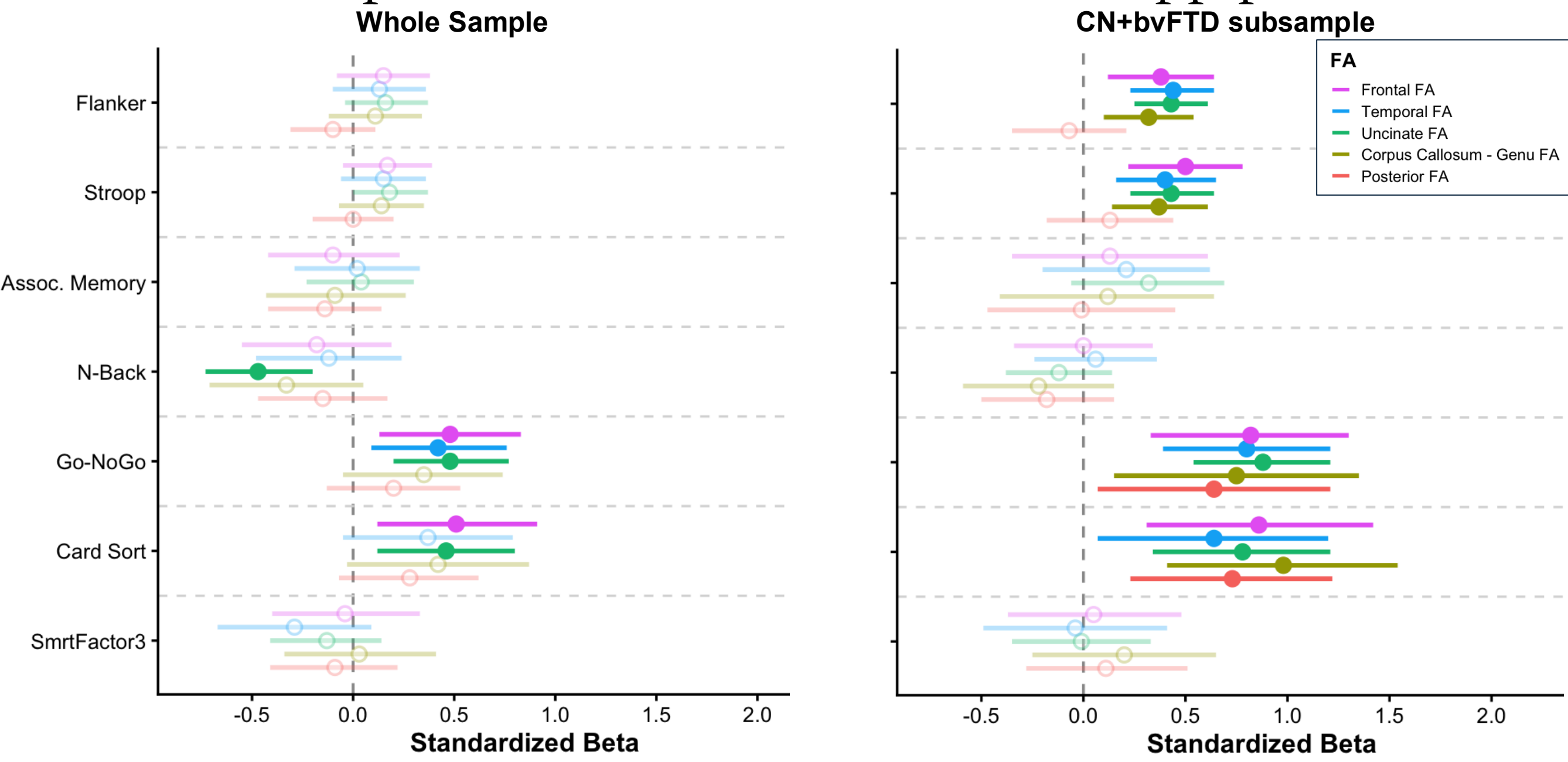
MCI=Mild cognitive impairment; FTLDCDR=frontotemporal lobar degeneration; Syndromes include behavioral variant FTD (bvFTD), corticobasal syndrome (CBS), logopenic variant primary progressive aphasia (lvPPA), nonfluent variant PPA (nfvPPA), primary supranuclear palsy (PSP), and semantic dementia (SD)

## Results

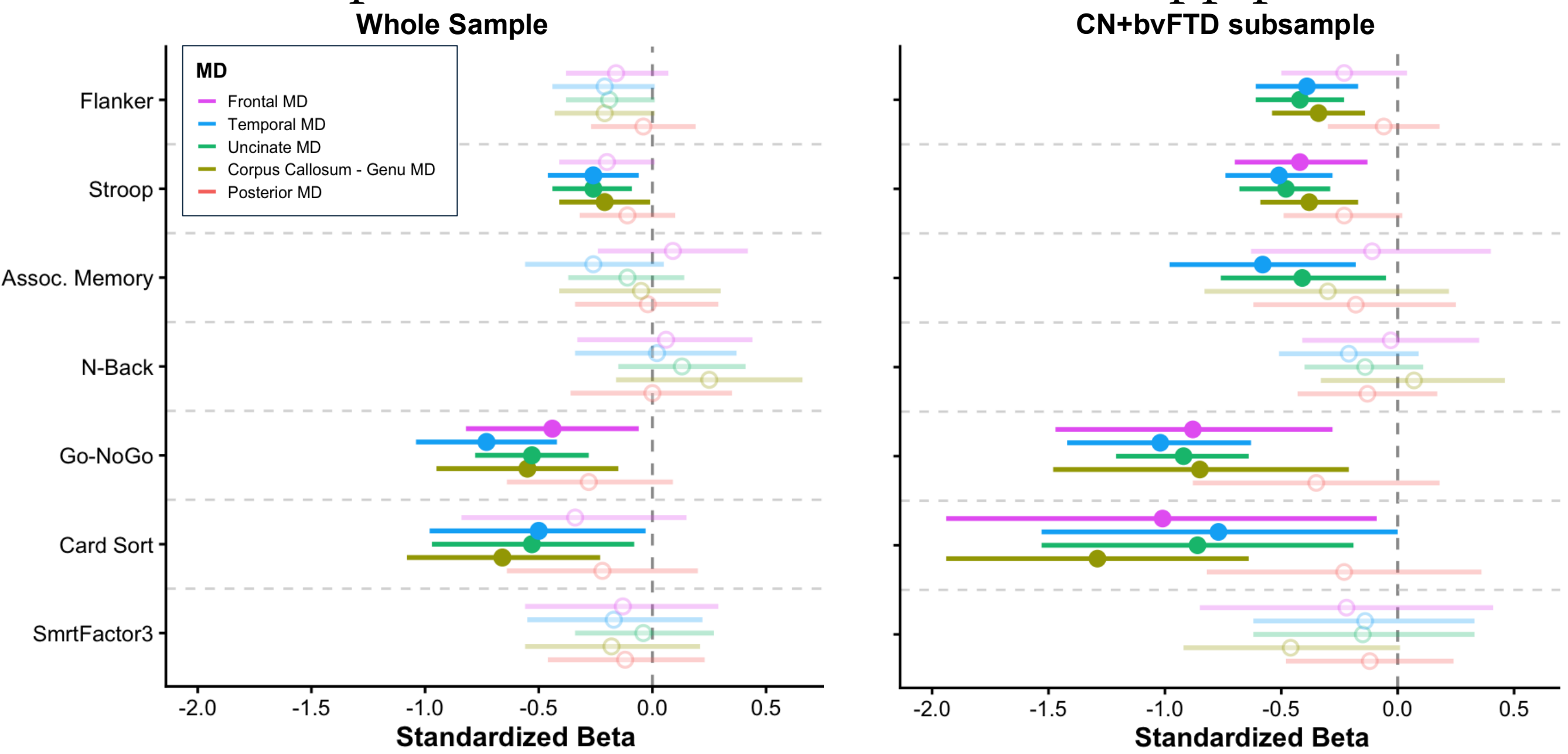
### Brain volume is broadly associated with mApp performance



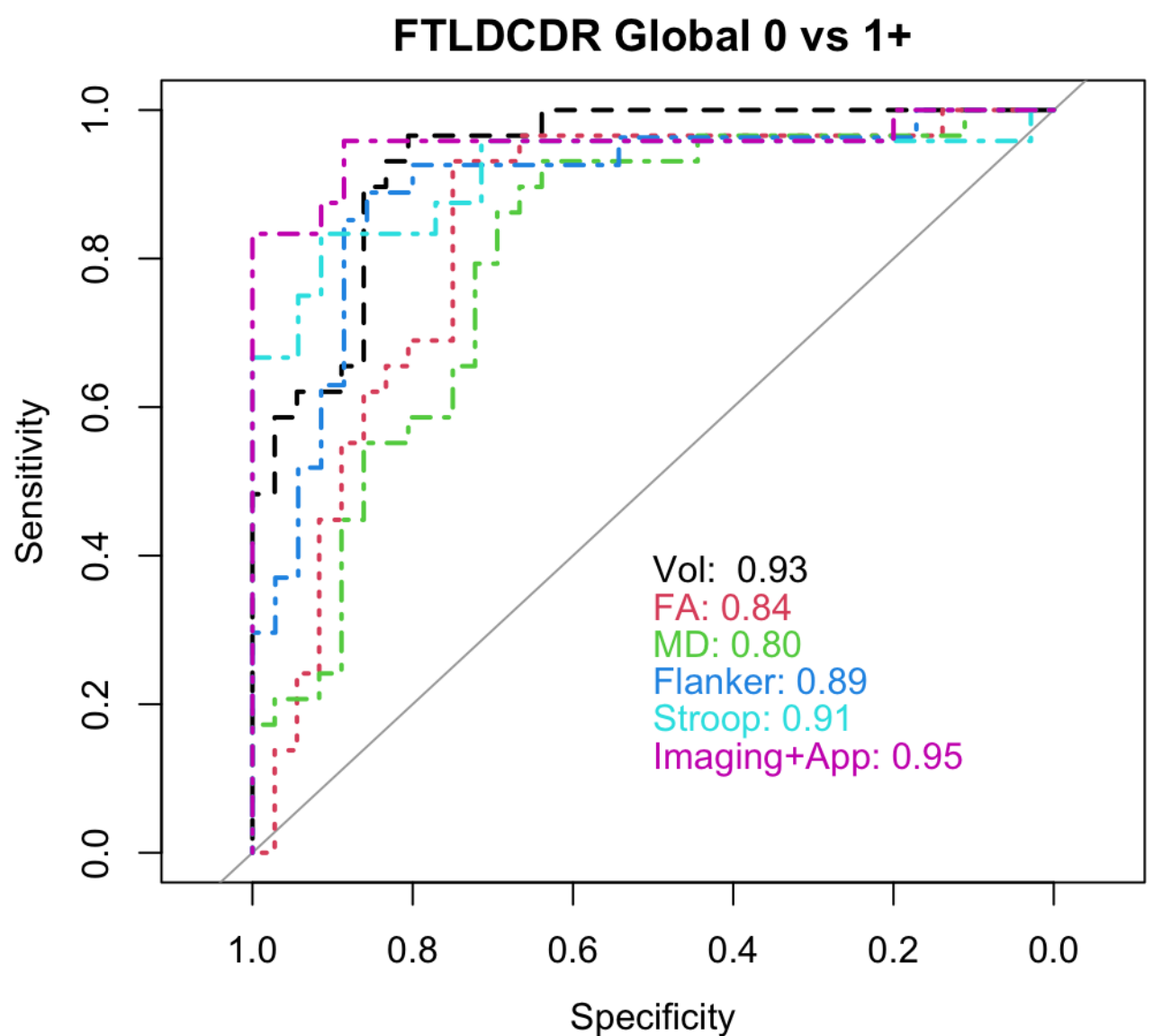
### Frontotemporal FA is associated with mApp performance



### Frontotemporal MD is associated with mApp performance



### mApp improves classification of impairment over imaging alone



## Discussion

- Remotely delivered cognitive assessments reflect alterations in brain volume and WM microstructure
- Frontotemporal WM structural integrity is associated with performance on executive functioning tasks
- mApp performs commensurately with imaging in diagnostic classification of disease severity
- mApp performance adds discriminative value to imaging
- Results support remote cognitive assessment as a clinically meaningful biomarker and its potential use in clinical trials within neurodegenerative disease<sup>4-5</sup>

## References

- Dhanam, S., Sanderson-Cimino, M., Taylor, J. C., Paolillo, E. W., Fregly, R., Kwang, W., Maruff, P., Wise, A., Heuer, H. W., Forsberg, L. K., Kramer, J. H., Boeve, B. F., Rosen, H. J., Mackin, R. S., Weiner, M. W., Nosheny, R. L., Boxer, A. L., Staffaroni, A. M., & the Brain Health Registry (2026). Remote, self-administered, smartphone cognitive testing in a registry-based cohort: Feasibility, reliability, and validity findings. *Alzheimer's & dementia : the journal of the Alzheimer's Association*, 22(6), e71580.
- Taylor, J. C., Heuer, H. W., Clark, A. L., Wise, A. B., Manooch, M., Forsberg, L., Mester, C., Rao, M., Brushaber, D., Kramer, J., Welch, A. E., Kornak, J., Kremers, W., Appleby, B., Dickerson, B. C., Domoto-Reilly, K., Fields, J. A., Ghoshal, N., Graff-Radford, N., ... Staffaroni, A. M. (2023). Feasibility and acceptability of remote smartphone cognitive testing in frontotemporal dementia research. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring*, 15(2), e12423.
- Staffaroni, A. M., Clark, A. L., Taylor, J. C., Heuer, H. W., Sanderson-Cimino, M., Wise, A. B., Dhanam, S., Cobigo, Y., Wolf, A., Manooch, M., Forsberg, L., Mester, C., Rankin, K. P., Appleby, B. S., Bayram, E., Bozoki, A., Clark, D., Darby, R. R., Domoto-Reilly, K., ... ALLFTD Consortium. (2024). Reliability and Validity of Smartphone Cognitive Testing for Frontotemporal Lobar Degeneration. *JAMA Network Open*, 7(4), e244266.
- Staffaroni, A. M., Tsou, E., Taylor, J., Boxer, A. L., & Possin, K. L. (2020). Digital Cognitive Assessments for Dementia. *Practical Neurology (Fort Washington, Pa.)*, 20(2), 24–45.
- Watson, J. L., Ryan, L., Silverberg, N., Cahan, V., & Bernard, M. A. (2014). Obstacles And Opportunities In Alzheimer's Clinical Trial Recruitment. *Health Affairs*, 33(4), 574–579.

## Funding

This study was supported by NIH-NIA grants U19AG063911-02, R01AG077557, K23AG061253, R01AG032289, R01AG048234, UCSF ADRC P30AG062422, and R01AG072475, as well as NIH-NINDS grant UF1NS100608. Additional funding was provided by the Bluefield Project to Cure FTD and the Larry L. Hillblom Foundation (2024-A-001-CTR; PI: KBC), with prior support from the Hillblom Foundation

Contact: ashley.heywood@ucsf.edu

