

Introduction

- Individuals with Down syndrome (DS) carry a genetic risk for developing Alzheimer's disease (AD), exhibiting early and accelerated accumulation of both beta-amyloid plaques and neurofibrillary tau tangles.
- Previous work investigated amyloid positivity prevalence across ages and thresholds in DS (Krasny 2024).
- New processing techniques for florbetapir PET and evidence for early PiB PET amyloid in the striatum warrant updated characterization of amyloid prevalence.

Objective

- This work investigated the baseline distribution and longitudinal trajectories of regional amyloid positivity across age and cognitive markers in adults with DS.

Methods

- Longitudinal amyloid PET and cognitive data were collected for 353 adults from the Alzheimer Biomarkers Consortium – Down Syndrome (ABC-DS) study (Table 1).
- Centiloids (CL) were calculated for amyloid PET (PiB: whole cerebellum reference; florbetapir: white matter reference). Average striatum SUVR was calculated for PiB.
- Amyloid status was determined using published cutoffs (Centiloids: 18.1 CL; Striatum: 1.12 SUVR).
- Modified Cued Recall Test (mCRT) scores were collected to assess episodic memory. Cognitive status was determined through case consensus conference.
- Participants were grouped by 5-year age increments, and prevalence was calculated for amyloid and impairment:

$$\text{Positivity Prevalence} = 100 \times \frac{\text{Number of positive participants}}{\text{Size of age group}}$$

Table 1 – Participant demographics.

	Entire Cohort	PiB Cohort	Florbetapir Cohort	p-value
Sample size [n]	353	231	122	N/A
Age at baseline, mean (SD) [yrs]	41.6 (9.6)	38.4 (8.4)	47.5 (8.9)	<0.001***
Female [n (%)]	151 (42.8)	107 (46.3)	44 (36.1)	0.070
Aβ scans [n]	353 298	231 176	122 122	N/A
Baseline Follow-up				
Average CL at baseline (SD)	28.6 (41.0)	16.1 (29.5)	52.4 (48.6)	<0.001***
mCRT tests [n]	335 281	221 173	114 108	N/A
Baseline Follow-up				
Average mCRT at baseline (SD) [0-36]	29.6 (9.0)	31.1 (7.4)	26.7 (11.0)	<0.001***

Results

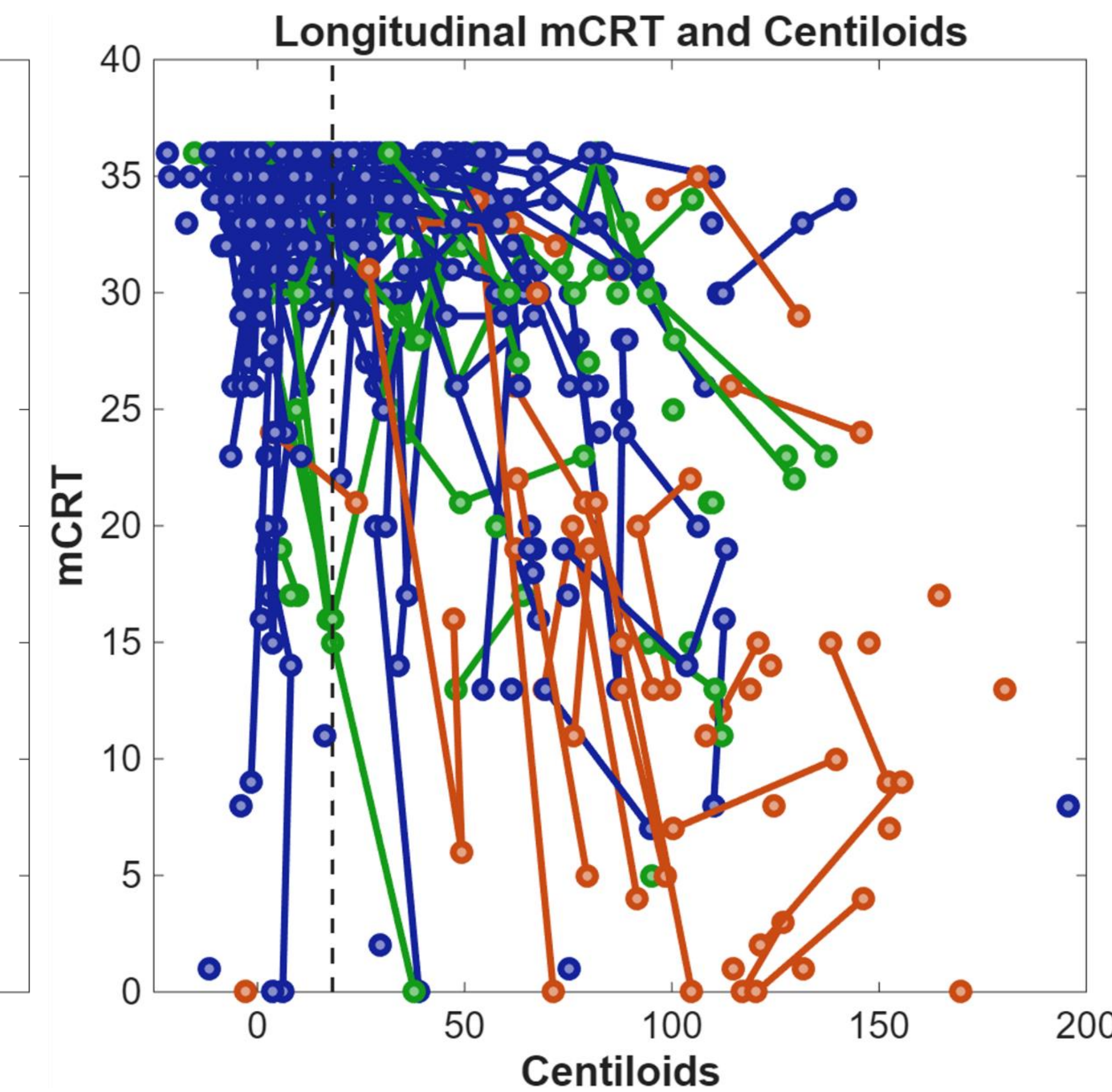
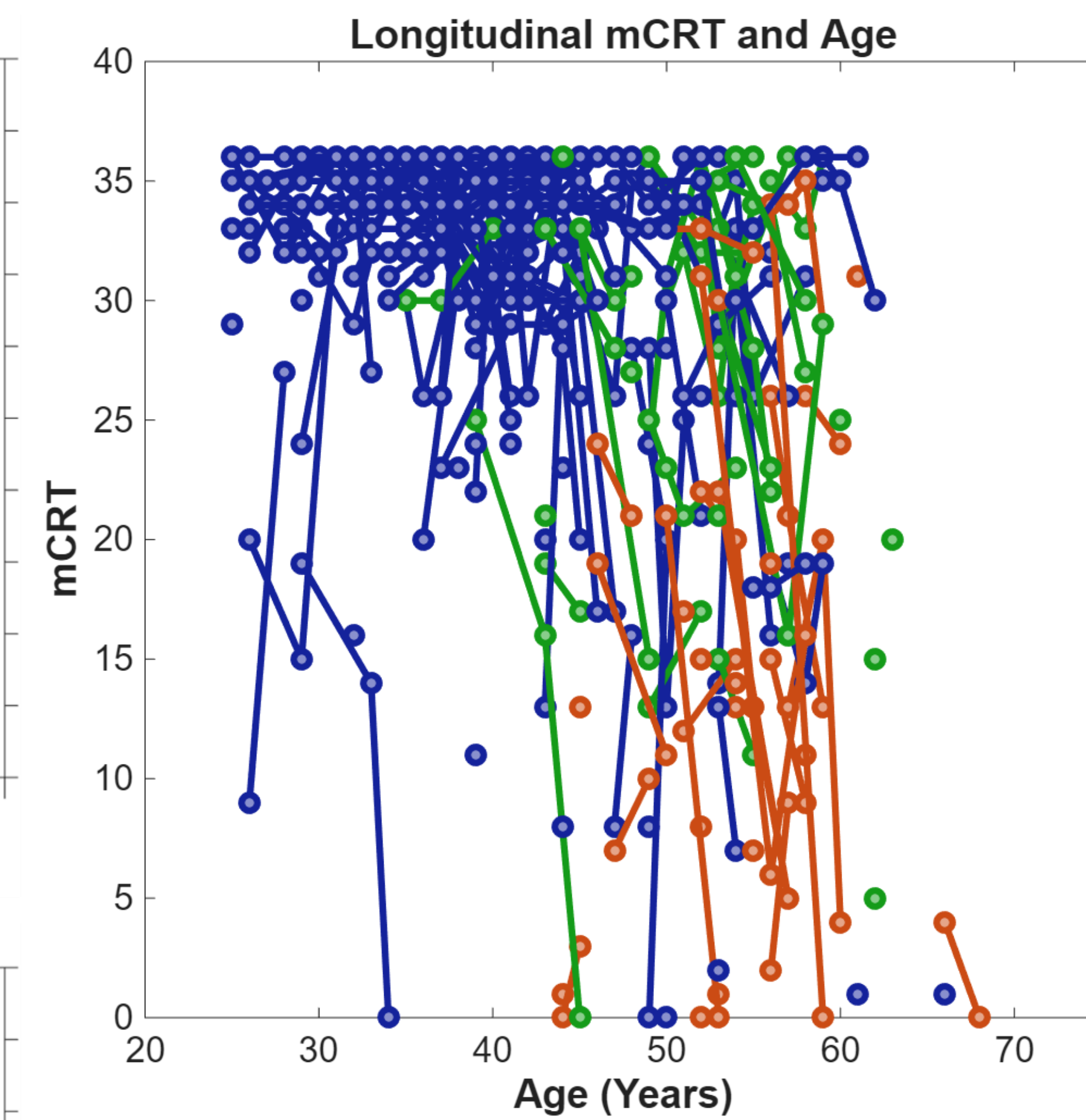
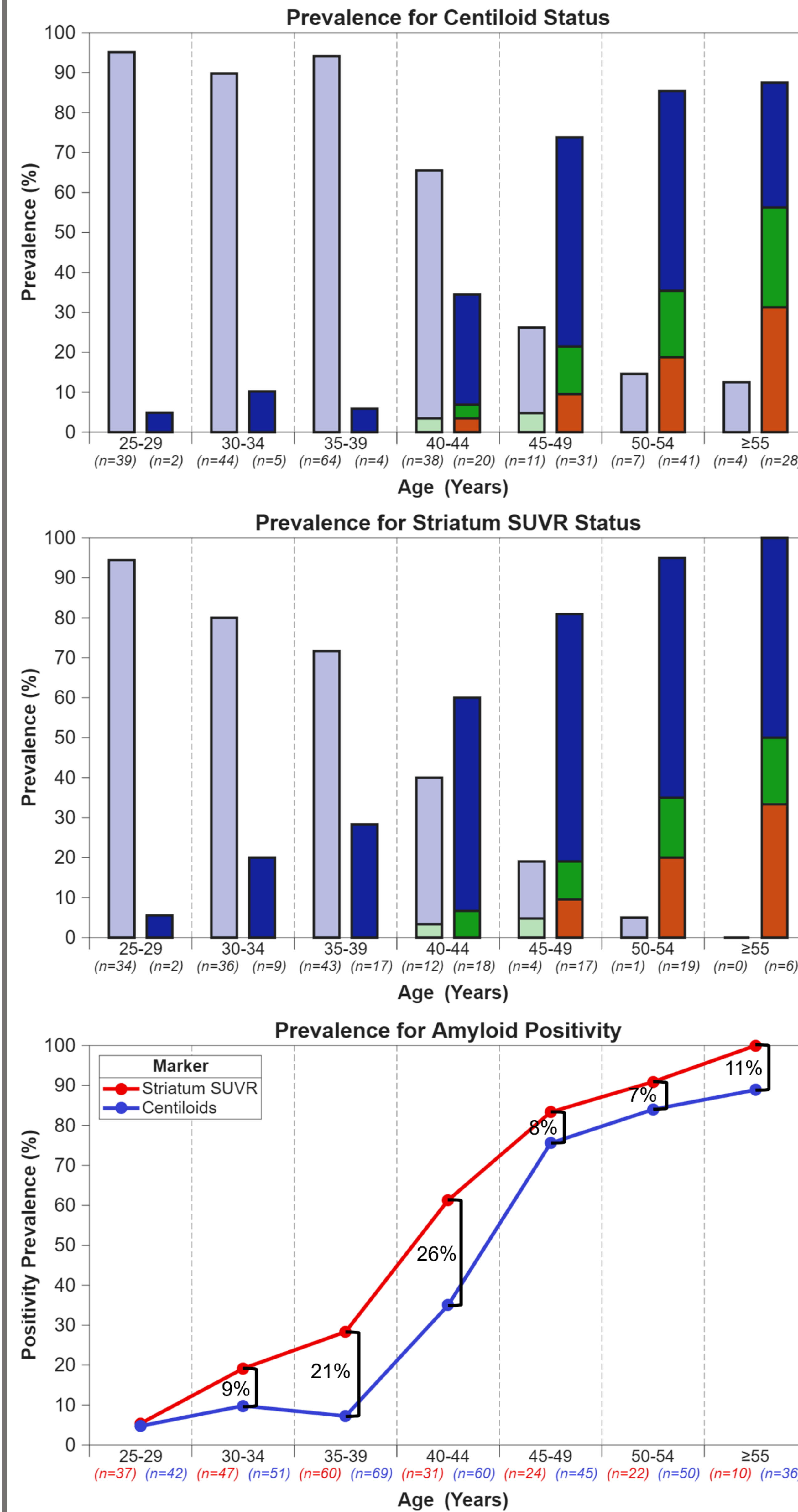


Figure 2 – Longitudinal mCRT trajectories plotted against age (left) and Centiloids (right). Correlation analysis between Centiloids and baseline mCRT yielded a Pearson correlation coefficient (PCC) of -0.61***. Additionally, the linear mixed effects model $mCRT \sim CL + (1 | \text{Participant})$ was applied:
Intercept = 33.2 ***
 $\beta_1 = -0.13$ ***

Abbreviations
CS – Cognitively stable
MCI – Mild cognitive impairment
Dem. – Dementia
CL – Centiloid
Str – Striatum

Figure 1 – Centiloid status prevalence (top) and striatum SUVR status prevalence (middle). The amyloid negative group (light bar in each age group) shows a steady decline in prevalence, with nearly all participants in the CS group. The amyloid positive group shows a steady increase, with a greater proportion of participants with MCI and dementia in each subsequent age group. CS participants make up the majority of the amyloid positive group in all age groups, except the ≥55 year grouping. The amyloid positive group becomes the majority earlier for the striatum (40-44 year grouping) than Centiloids (45-49 year grouping). The bottom figure overlays Centiloid and striatum SUVR positivity prevalence and displays their difference ($\text{Prevalence}_{\text{Str}} - \text{Prevalence}_{\text{CL}}$) for each age group. Individuals with an “Undetermined” cognitive status are not displayed here.

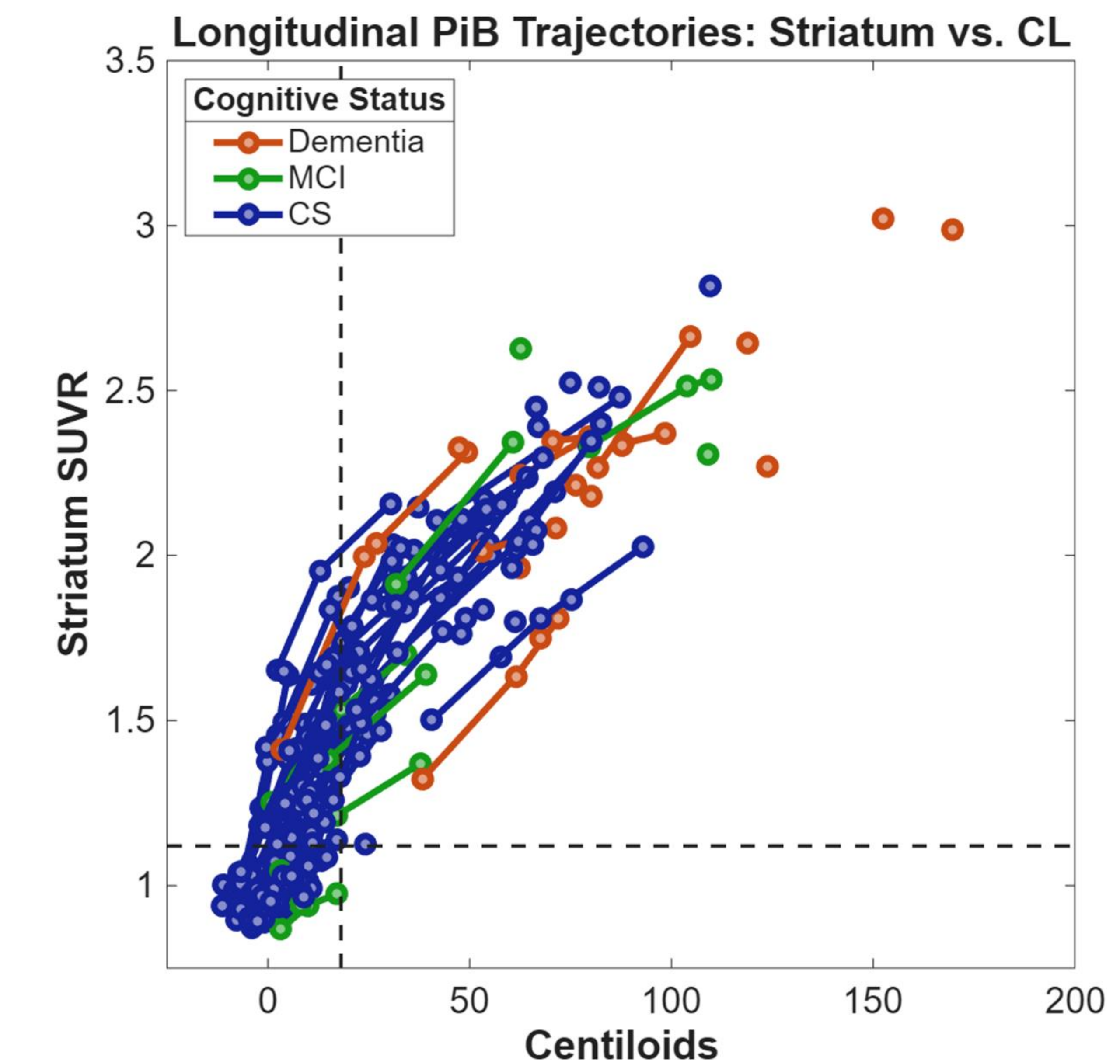


Figure 3 – Longitudinal PiB striatum SUVR trajectories plotted against Centiloids. Participant trajectories suggest consistently earlier stratum positivity before proceeding to Centiloid positivity.

Conclusions

- The DS population demonstrates high prevalence of amyloid positivity, particularly when using PiB striatum SUVR.
- The continued characterization of AD pathology in DS is critical for improving health outcomes in this population and developing a holistic understanding of AD.

Acknowledgements

- We would like to thank all the participants and their families for their generous and ongoing contributions to the ABC-DS project.
- This work was supported by U01 AG051406, U01 AG051412, U19 AG068054, S10 OD025245, & P50HD105353.