

Longitudinal brain metabolic decline in isolated REM sleep behavior disorder

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BACKGROUND

- Isolated REM sleep behavior disorder (iRBD) is a prodromal synucleinopathy with high risk of progression to cognitive impairment due to DLB and PD.
- FDG PET provides an in vivo proxy of glucose metabolism and may detect neurodegenerative changes before overt cognitive impairment.

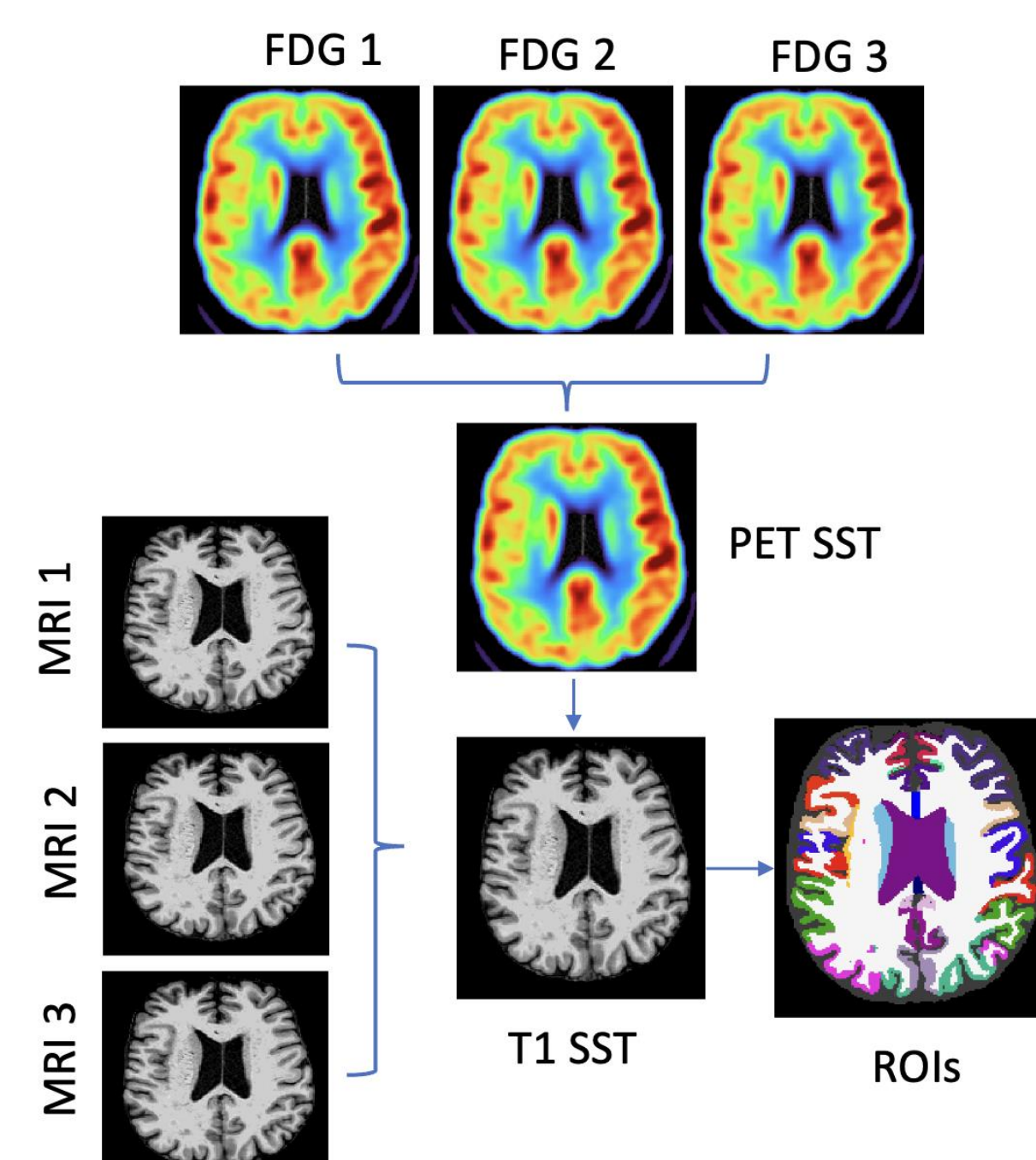
METHODS

- Participants:** 27 iRBD vs 200 CU; ≥ 2 FDG-PET visits; 620 total scans

Variable	CU (n=200)	RBD (n=27)	p
Baseline Age	65.1 [58.4, 71.6]	64.7 [61.8, 73.5]	0.7
MMSE	29.0 [28.0, 30.0]	29.0 [28.0, 30.0]	0.9
Follow-up, years	5.3 [2.6, 7.7]	4.0 [1.6, 7.1]	0.1
Male, n (%)	162 (81%)	21 (78%)	0.8
APOE $\epsilon 4$ positive, n (%)	63 (32%)	7 (28%)	0.8

- Neuroimaging:** in-house MCALT pipeline with longitudinal within-subject templates.

Overview of FDG pipeline

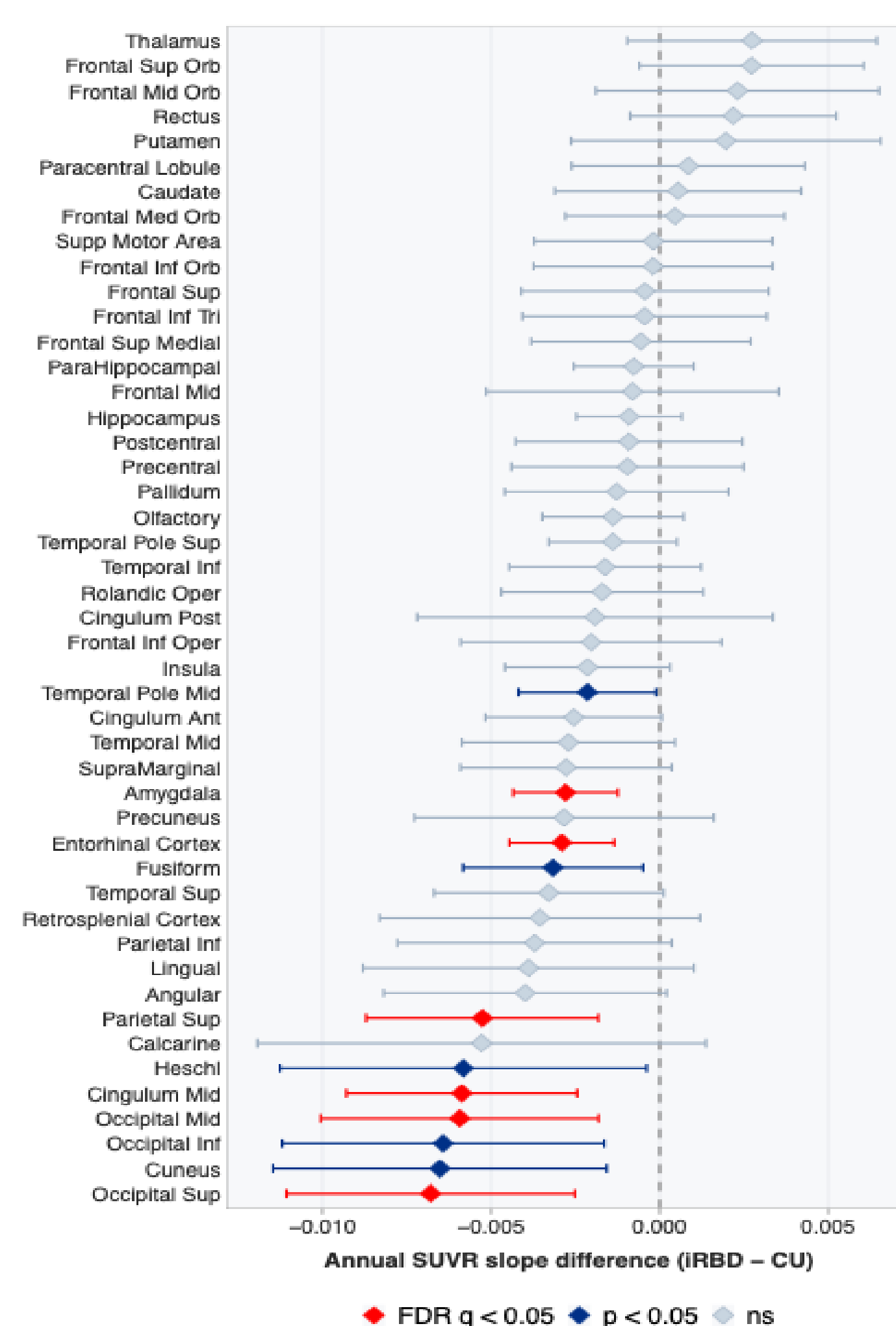


RESULTS

LINEAR MIXED EFFECT MODEL

- Analysis:** Random-intercept linear mixed-effects, $SUVr \sim \text{time} \times \text{group} + \text{age} + (1 | \text{subject})$.
- Findings:** iRBD showed accelerated FDG-PET decline relative to CU across a posterior-limbic network, 6 of 47 ROIs survived FDR correction (all $q < 0.05$, all $\beta < 0$)

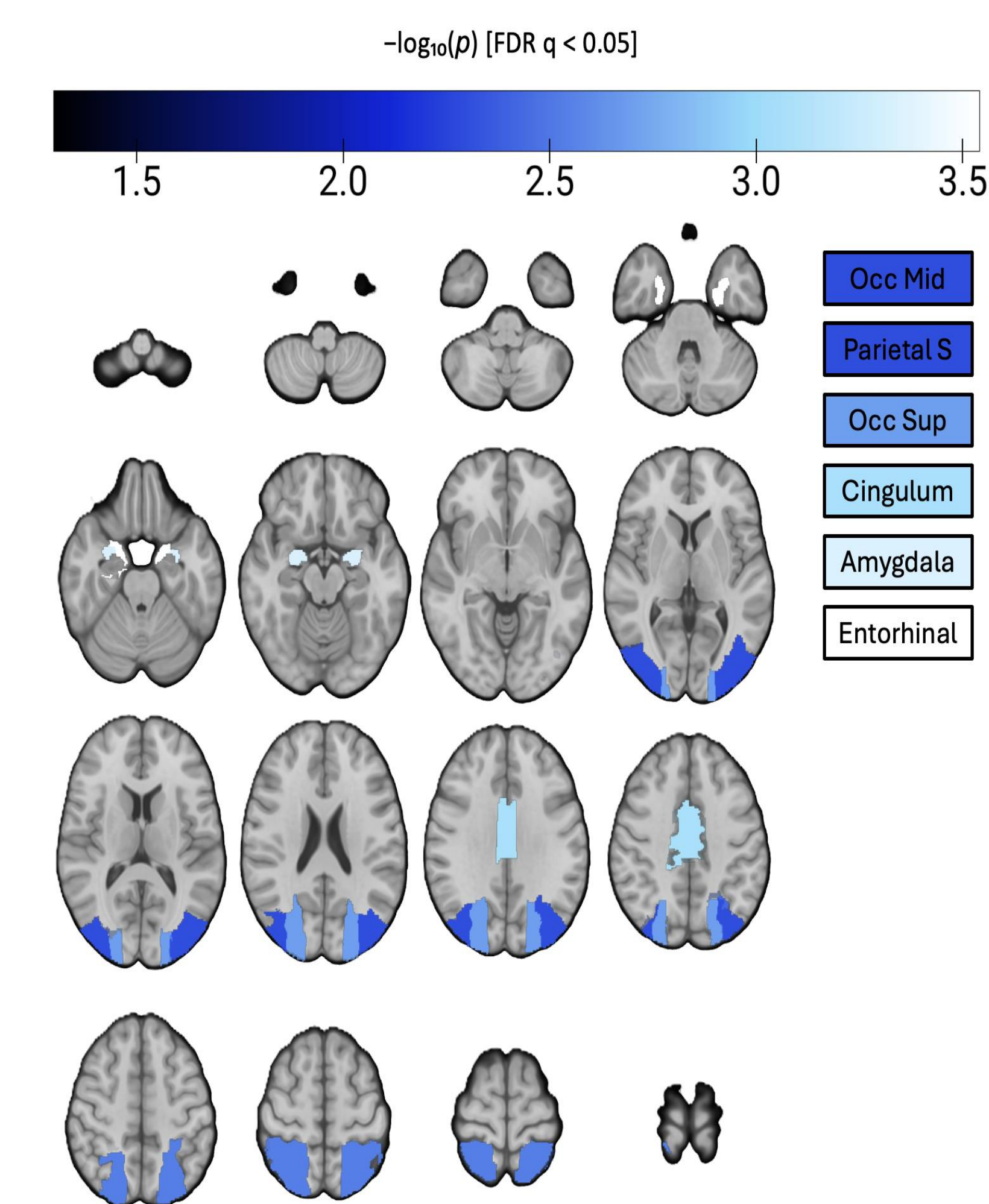
Forest plot of regional models



- Each point represents the estimated annual FDG SUVR slope difference (iRBD - CU) for an ROI. Errors bars indicate 95% confidence intervals.
- Sensitivity analysis:** Findings remained significant (FDR $q < 0.05$) after controlling for volume as a fixed effect.

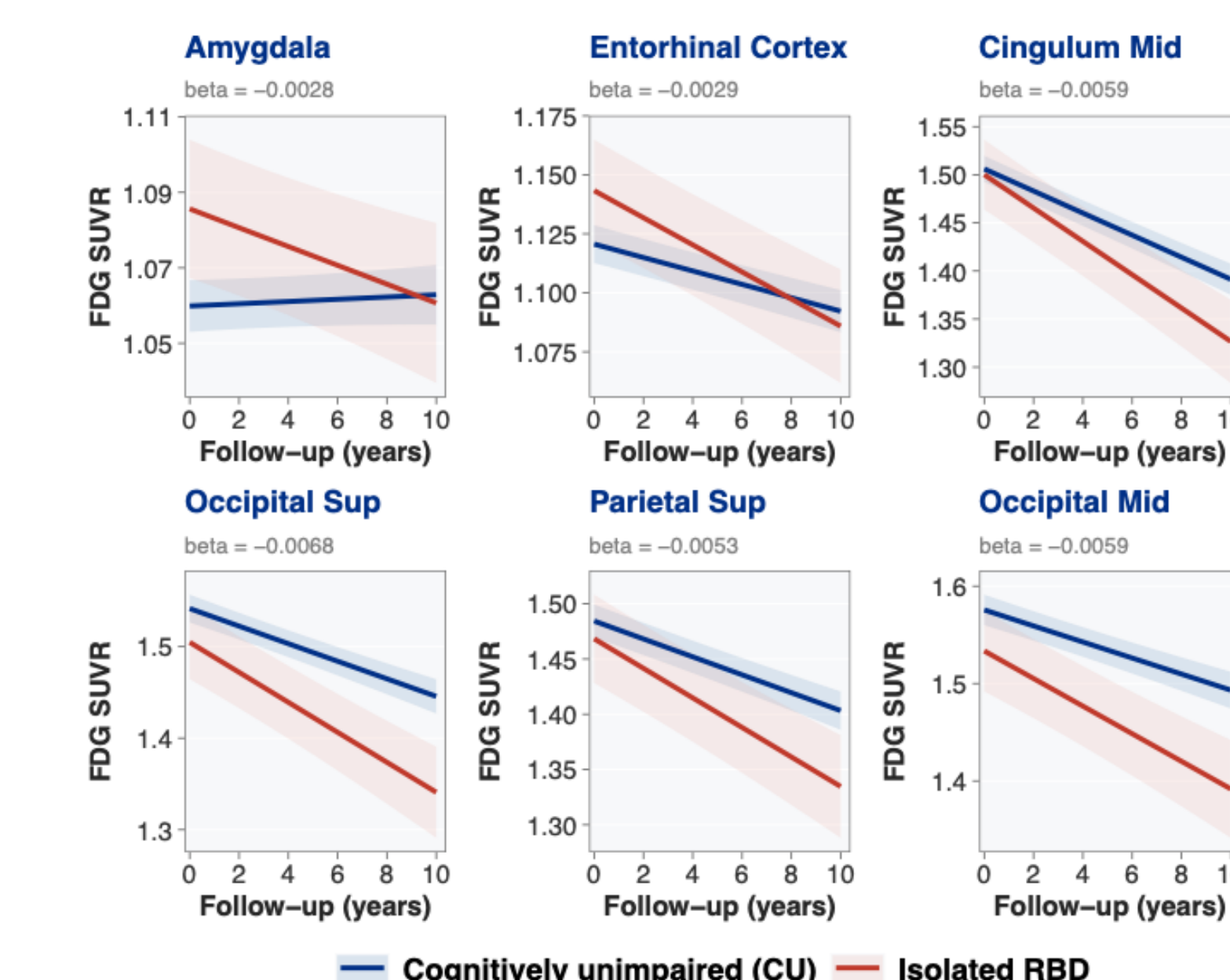
TOPOGRAPHY OF FDG DECLINE

Posterior-limbic hypometabolism



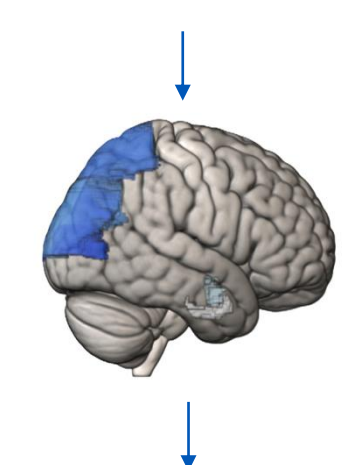
- Estimated marginal FDG SUVR trajectories for the 6 FDR-significant regions, derived from random-intercept LME models at mean baseline age. Shaded bands = 95% CI.

Trajectories of FDG decline over time



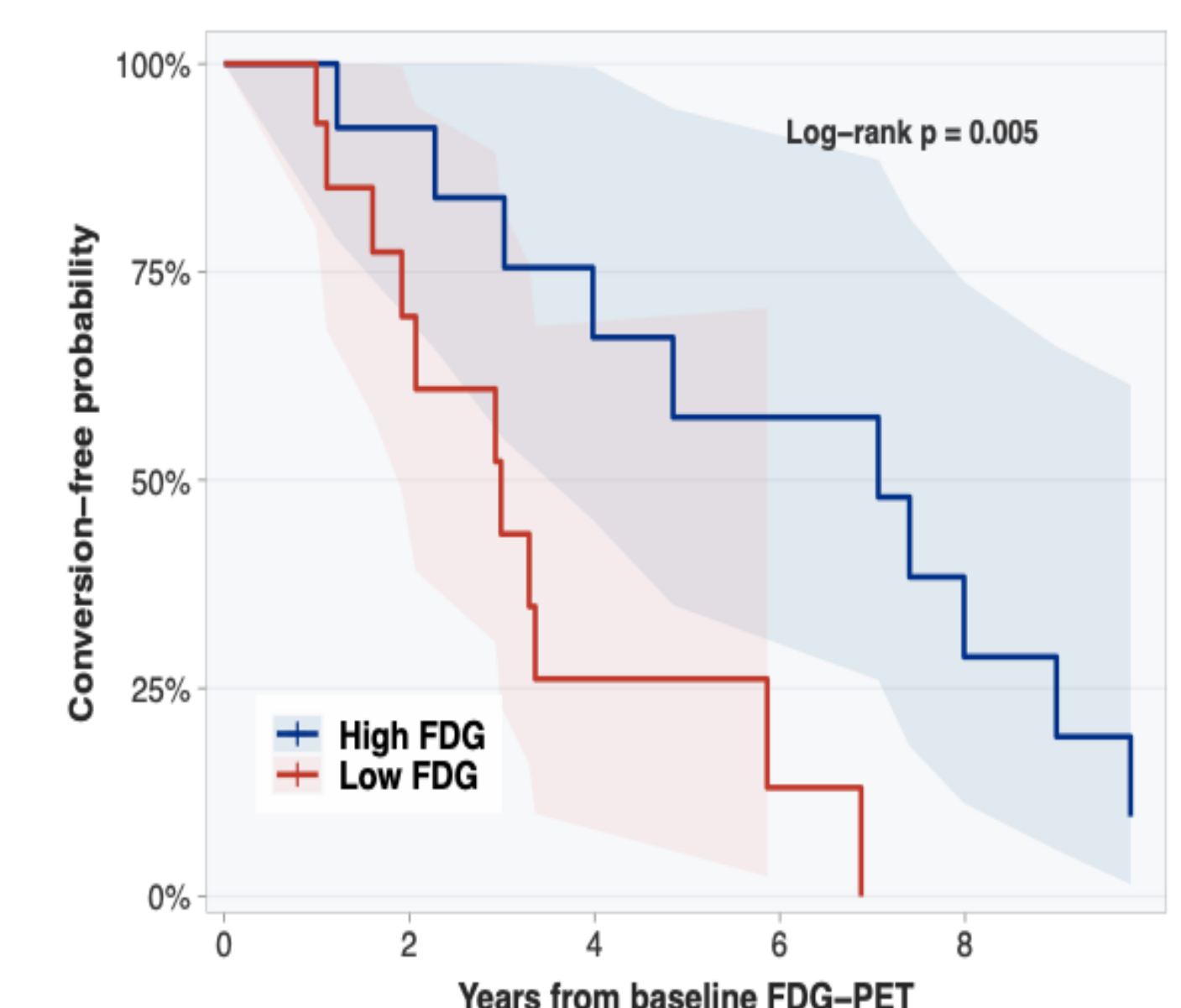
COX REGRESSION MODEL

- 75% of iRBD converted over a median 3.98 years from FDG visit.
- An FDG meta-ROI was derived from the LMEs and used as the predictor for survival analyses



- Lower baseline meta-ROI FDG predicted faster phenoconversion
- HR = 2.54 (95% CI 1.30–4.97, $p = 0.007$) per 1-SD worsening.

Kaplan-Meier plots by FDG



DISCUSSION

- Longitudinal FDG-PET reveals a posterior-limbic hypometabolic signature in iRBD.
- The FDG meta-ROI predicted subsequent clinical progression, supporting FDG-PET as a promising biomarker of prodromal Lewy body disease.