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Introduction

- Neuroimaging-based “brain age” models aim to capture chronological age variability by estimating biological brain aging from structural MRI data
- Translation of brain age models into broader clinical and population settings remains limited

Methods

Study Cohort Characteristics

	NACC training	NACC evaluation	SHS
N	2713	5460	703
age	70.5±9.0	71.3±10.4	72.9±5.8
Sex, n (male/female)	906/1807	2189/3271	222/481
CDR>0	338	2783	
3MSE			88.6±11.4
Diabetes, n(%)			351 (49.9%)
eGFR (ml/min)			60.8±22.6
Hypertension, n(%)			573 (81.5%)
BMI			31.4±6.5

- A feedforward multilayer perceptron (MLP) was developed to predict chronological age from SynthSeg-derived volumetric features.
- The final model was evaluated on the NACC test set and applied without modification to the full NACC cohort and the independent SHS cohort to assess external generalizability.

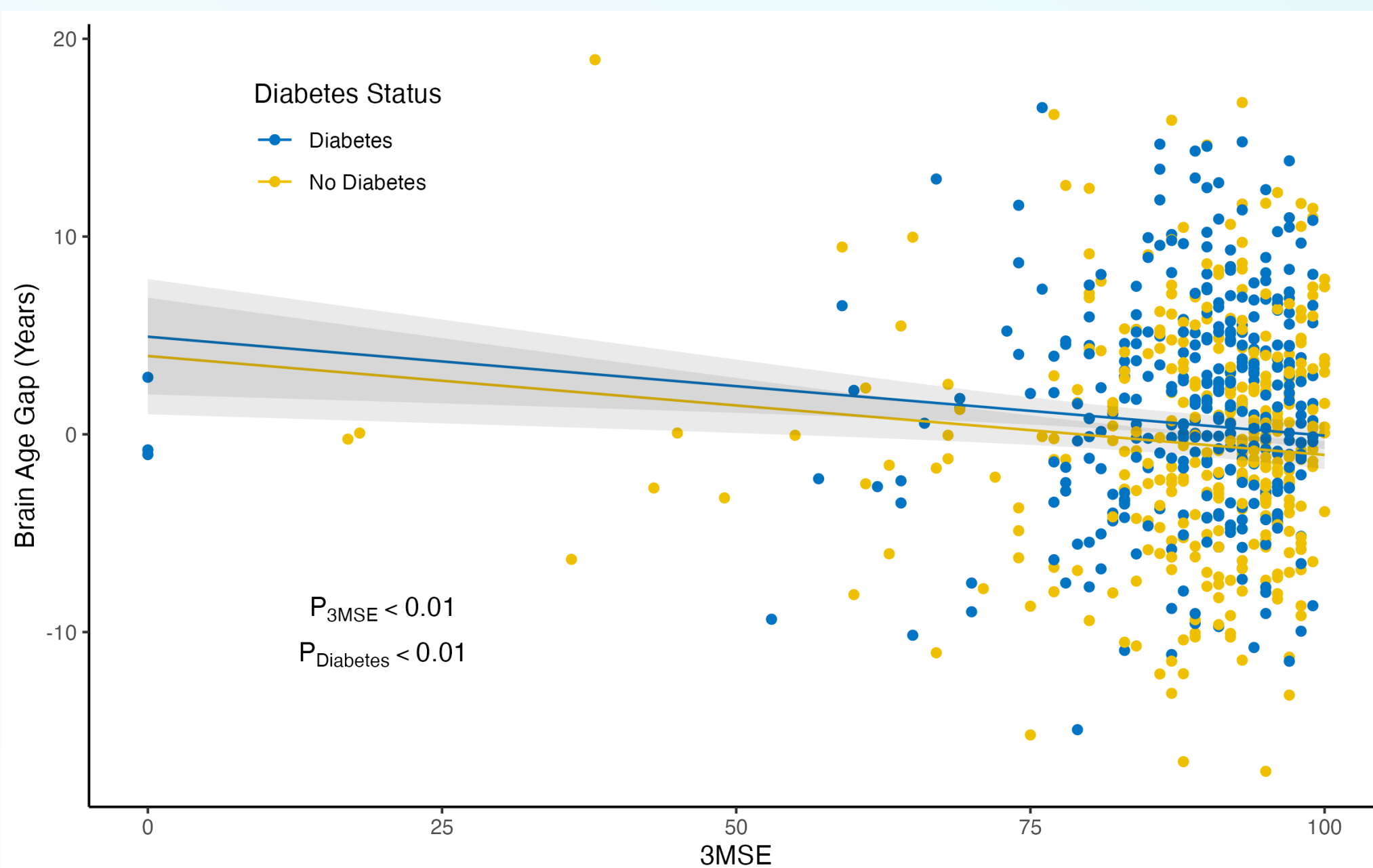
Discussion

- The model demonstrated comparable predictive accuracy across datasets, with similar mean absolute error observed in both cohorts
- The findings show that the relationship between the brain age gap (BAG) and cognitive performance is preserved in an independent population
- A key contribution of this work is the demonstration of model robustness across differences in imaging acquisition and cohort characteristics
- This study also contributes to the limited body of neuroimaging research in American Indian populations

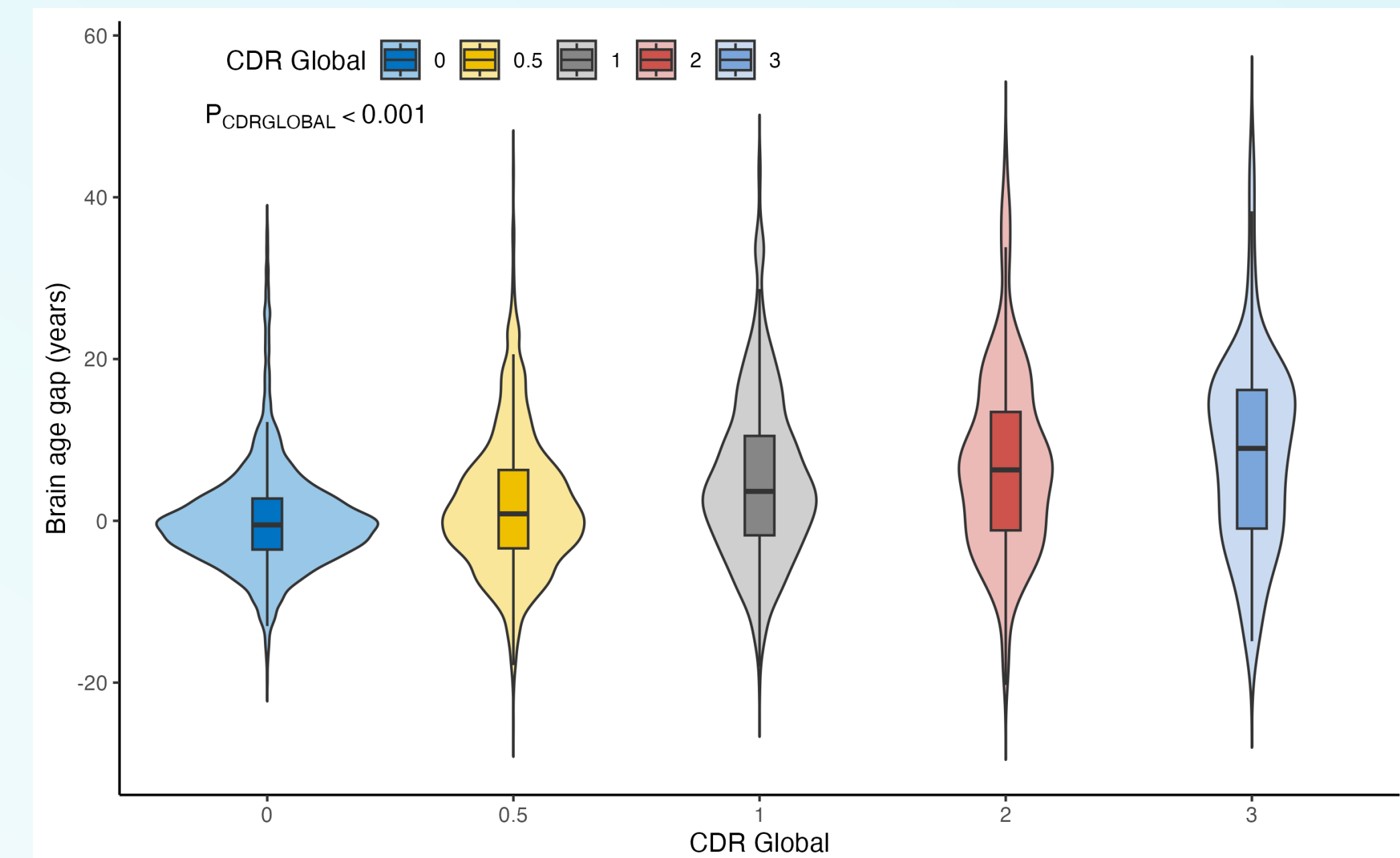
Results

term	estimate	std.error	statistic	p.value
(Intercept)	51.8	3.56	14.55	5.10E-42***
age	-0.59	0.037	-17.5	5.90E-57***
sex	1.86	0.38	4.94	9.95E-07***
education	-0.28	0.13	-2.21	0.027*
3MSE	-0.046	0.017	-2.77	0.006**
eGFR	-0.015	0.008	-1.82	0.069
diabetes	-1.08	0.36	-2.97	0.003**
hypertension	-0.67	0.47	-1.44	0.151
BMI	-0.044	0.029	-1.54	0.127

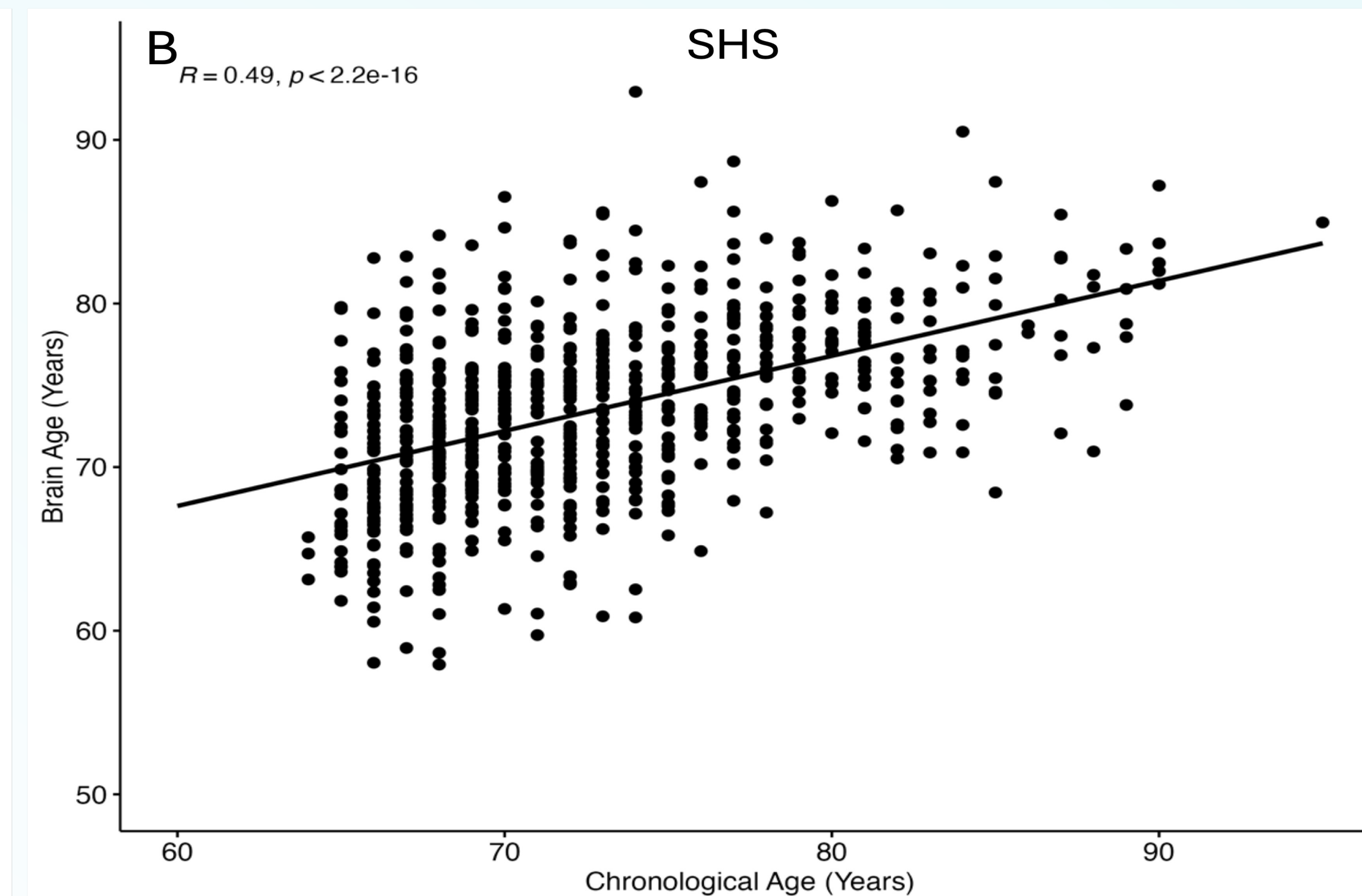
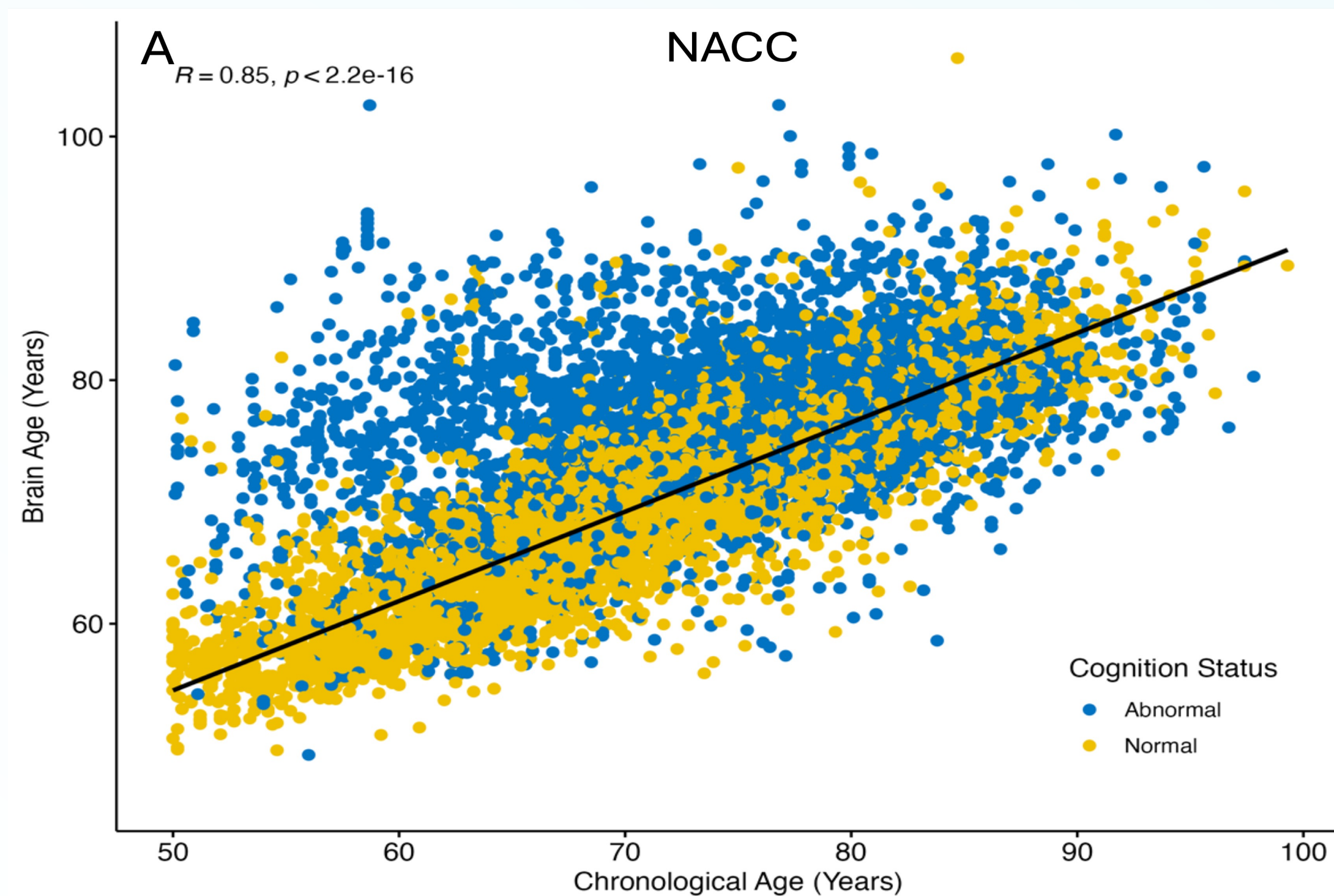
Multivariate linear regression model of brain age gap as a function of demographic and clinical variables



BAG was inversely associated with 3MSE scores. Participants with diabetes exhibited higher BAG and lower cognitive performance



Brain age gap increases with more advanced CDR rating



Predicted age from MRI versus chronological age in NACC (A) and SHS (B) cohorts