

Genetic influences on cerebral blood flow in early old age and associations with cognitive performance

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BACKGROUND

- Cerebral blood flow (CBF) is influenced by age and may predict future cognitive decline and neurodegenerative disease.
- Reported associations between gray matter CBF and cognitive performance are mixed, with more consistent associations evident in neurodegenerative disease.
- Gray matter CBF may be moderately heritable, although the genetic contribution may vary by brain region and age.

METHODS

Participants:

- 265 male twins in early old age from the Vietnam Era Twin Study of Aging (VETSA)

Sample Characteristics	
Age, years	72.74 (2.59)
Hx of smoking (Ever smoked)	60% (160)
Hypertension	64% (170)
Diabetes	29% (76)
Stroke	7.9% (21)
Education, years	14 (2.0)
APOE-ε4 carrier	33% (77)
Mild cognitive impairment (MCI)	13.9% (36)

Mean (SD); % (N)

Neuroimaging:

- 3D pcASL: labeling 1.8s, PLD 2.025s; TE=10.5ms, TR=4.87s, voxel size = 3.75x3.75x4 mm³
- CBF derived using FSL (v.6.0.7.18) Bayesian Inference for Arterial Spin Labeling (BASIL)
- 3D T1: TI = 600ms, flip angle = 8°, 1.2mm thickness
- Gray matter parcellations (Fig. 1) and partial volume estimates derived using FreeSurfer v.6.0 and sMRIPrep v.0.15.0

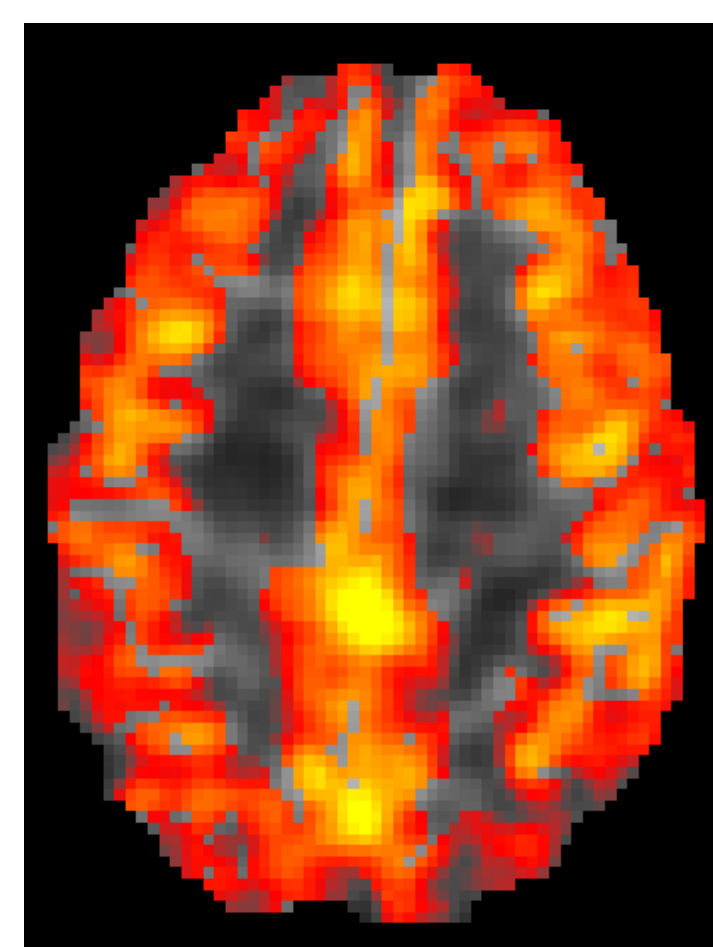


Figure 1: CBF measures were extracted from gray matter. Red to Yellow for increasing CBF signal.

Cognitive Domains:

- Episodic memory
- Executive function
- Visuospatial ability
- Processing speed
- Verbal fluency

Statistical Methods:

- Robust linear mixed effects (LME) models: CBF ~ cognition + age + hematocrit + scanner + (1|Family ID)
- Classical twin method to estimate heritability

RESULTS

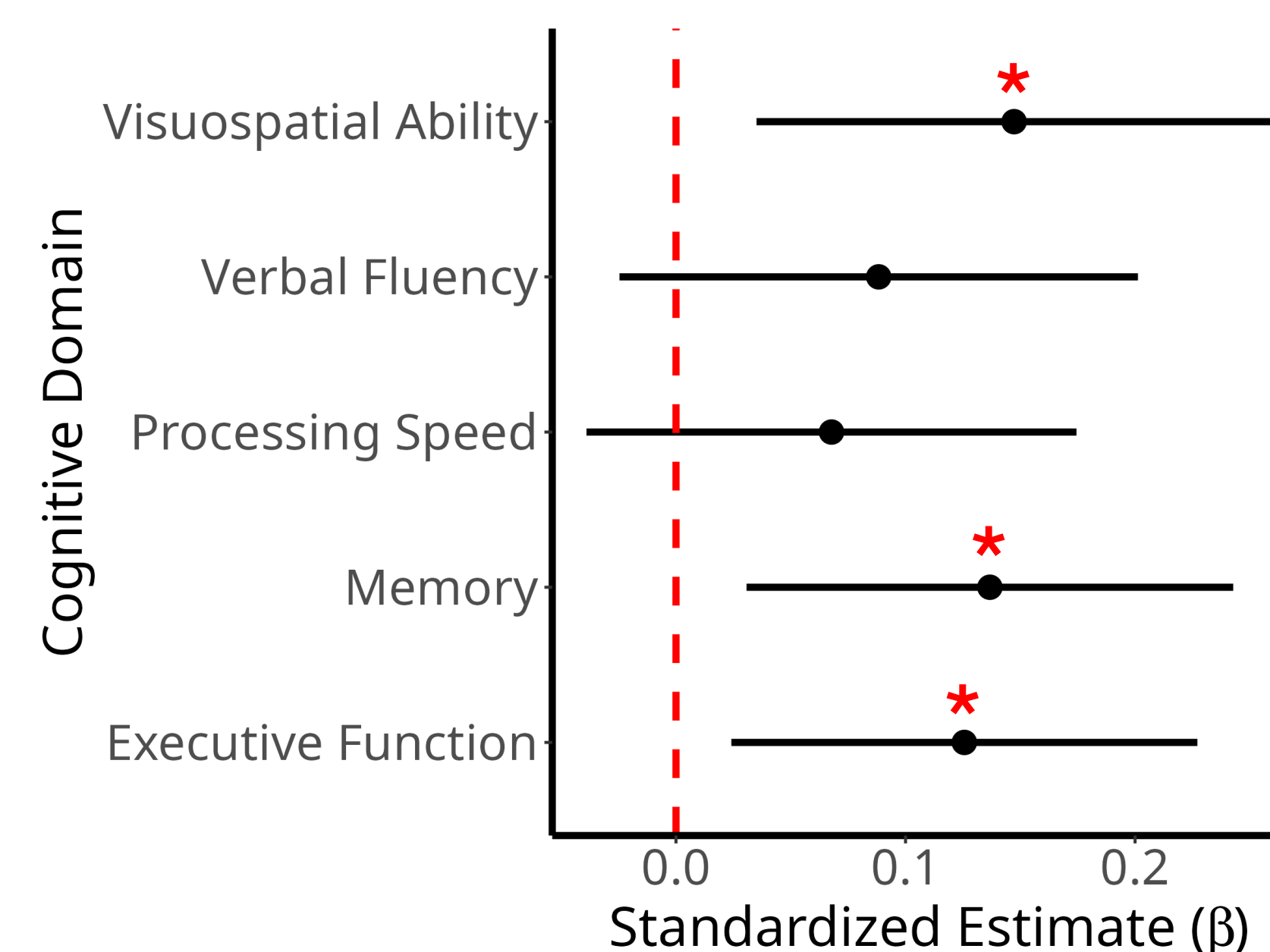


Figure 2: Associations between global gray matter CBF and cognitive domain scores. * = significant after FDR correction

- Better visuospatial ability, episodic memory, and executive function associated with higher global gray matter CBF (Fig. 2)
- There was no interaction with MCI status

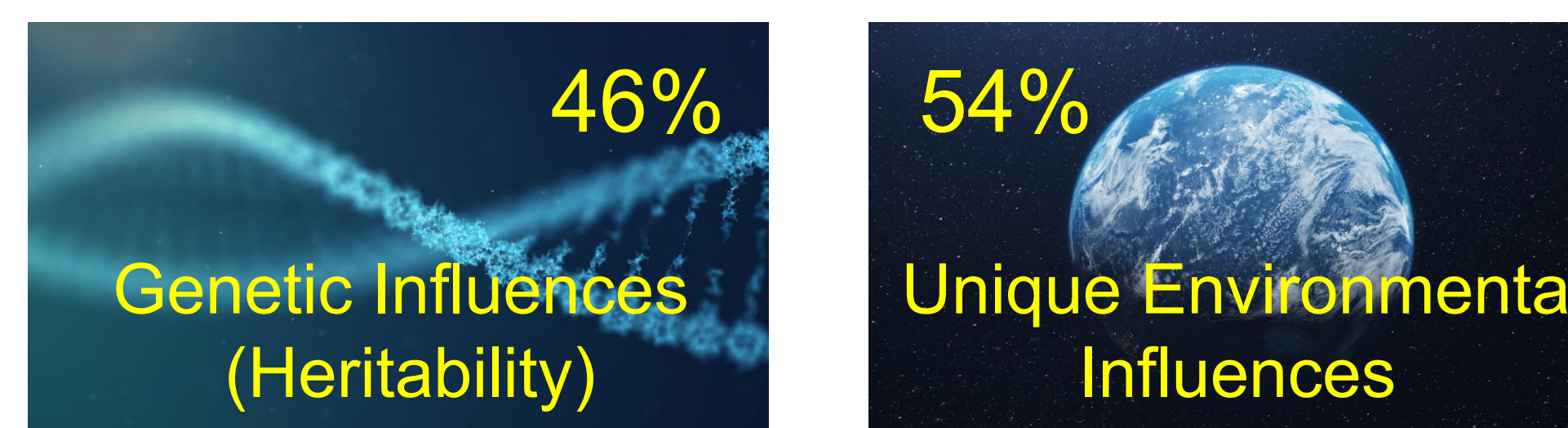


Figure 4: Genetic and environmental influences on global gray matter CBF

- Genetic influences accounted for 46% of the variance in global gray matter CBF (Fig. 4) and were largely consistent across regions (38% - 55%, pallidum 29%) (Fig. 5)

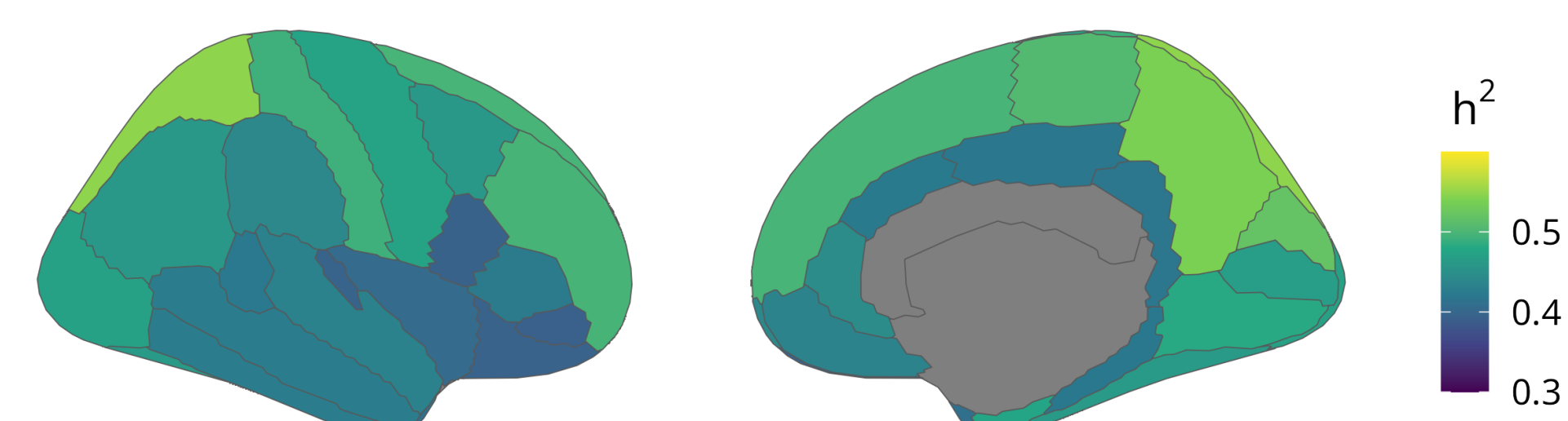


Figure 5: Genetic influences (heritability, h^2) on neocortical CBF across regions

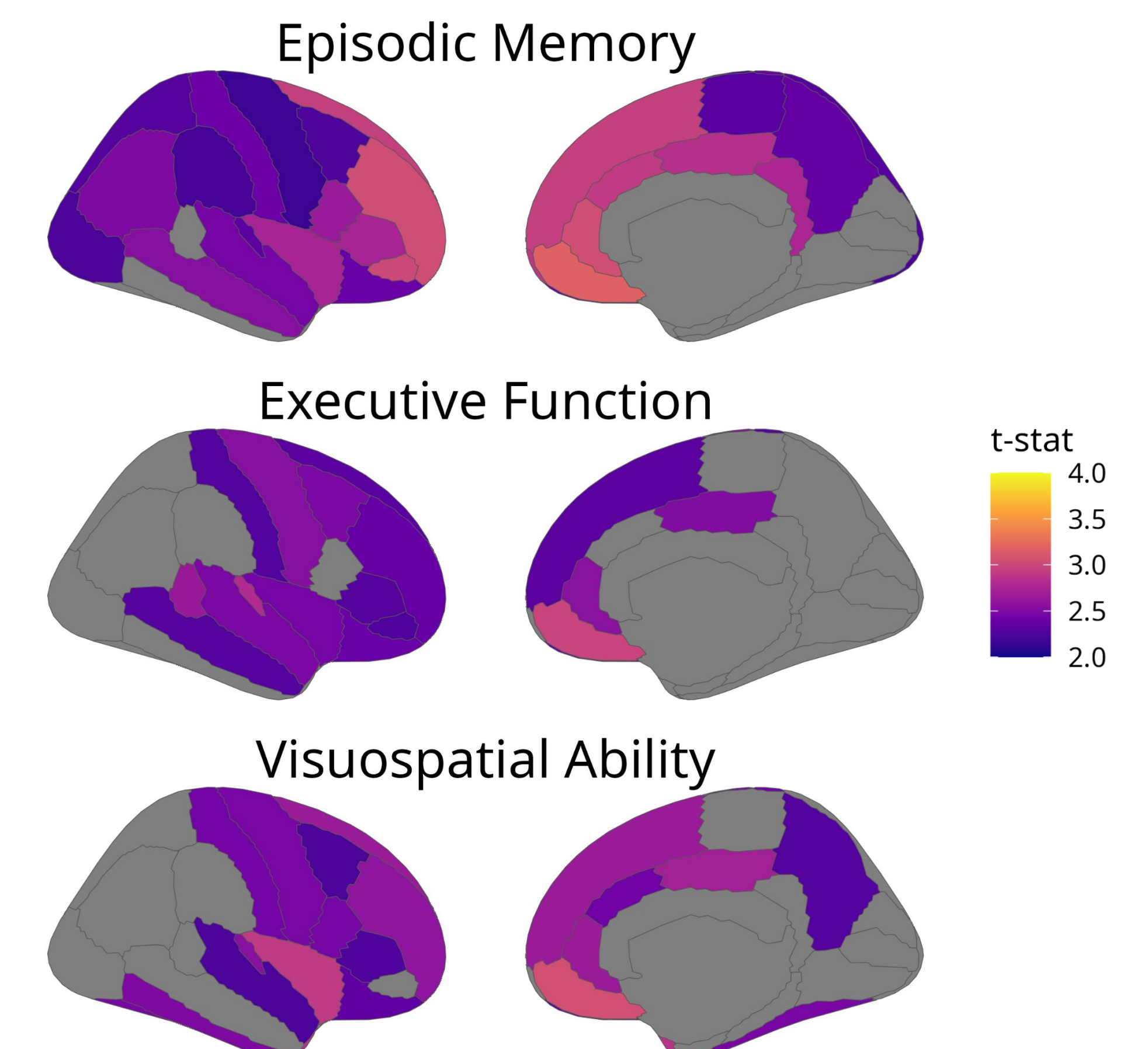


Figure 3: Regional neocortical gray matter CBF associations with cognitive domain scores

- Regionally, cognitive domains were associated with CBF in frontal, superior temporal, and insular cortex (Fig. 3)

CONCLUSIONS

- Higher CBF related to better cognitive performance across several domains, but notably not within mesial temporal regions
- Findings may reflect subtle contributions of cerebrovascular health that operate similarly across cognitive spectrum (i.e, in normal aging and MCI)
- Cerebrovascular risk profiles must take into account genetic and environmental factors
- Future work will examine the extent to which associations are jointly affected by genetic and environmental influences and explore the causal nature of relationships

Supported by NIA Grants: R01s AG076838, AG022381, AG050595, AG064955; and K01 AG063805

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