

INTRODUCTION

- **Extracranial carotid artery disease (ECAD)** occurs when fatty deposits, called plaques, clog the blood vessels that deliver blood to the brain and head.
- ECAD is predominantly evaluated clinically for stroke prevention, but is increasingly recognized as a potential **risk factor for Alzheimer's disease (AD)** and cognitive dysfunction [1-2]
- Understanding the relationship between ECAD and poorer cognitive outcomes may shed light into **preventive strategies**
- **This study aims to elucidate ECAD's impact on neurodegenerative changes through the investigation of brain morphology using 3T magnetic resonance imaging**

METHODS

- 127 participants 50-85 y.o with ≥ 2 cardiovascular risk factors and/or ECAD underwent neurological MRI

Characteristic	N = 127
Age	72 (7)
Sex [Male]	66 (52%)
Education Years*	14.97 (2.54)
Race	
White	121 (95%)
Black or African American	1 (0.8%)
Asian	4 (3.1%)
Other	1 (0.8%)
Ethnicity	
Hispanic/Latino	15 (12%)
Not Hispanic/Latino	112 (88%)
Hypertension	83 (65%)
Diabetes	35 (28%)
Hyperlipidemia	97 (76%)
Smoking	64 (50%)
History of Stroke/TIA	21 (17%)
Coronary Artery Disease	44 (35%)
Peripheral Artery Disease	22 (17%)
CSVD Score**	
Lo CSVD [0-1]	80 (64%)
Hi CSVD [2-4]	45 (36%)
Carotid Stenosis %	
≤ 29	37 (29%)
30-49	20 (16%)
50-69	30 (24%)
≥ 70	40 (31%)

Continuous variables are presented as Mean(SD) and categorical variables as n(%). *Education available for N=124 in CAM. **CSVD score available for N=125 in CAM.

- 1mm³ T1-MPRAGE was processed using *FreeSurfer v7.3.2* automated cortical parcellation pipeline [3] and underwent manual correction of cortical boundaries
- Percent carotid stenosis was quantified via high-resolution angiography, and cerebral small vessel disease (cSVD) severity was graded 0-4 [4] by a neuroradiologist (RM)

Table 1. Demographic overview outlining key characteristics of the study cohort.

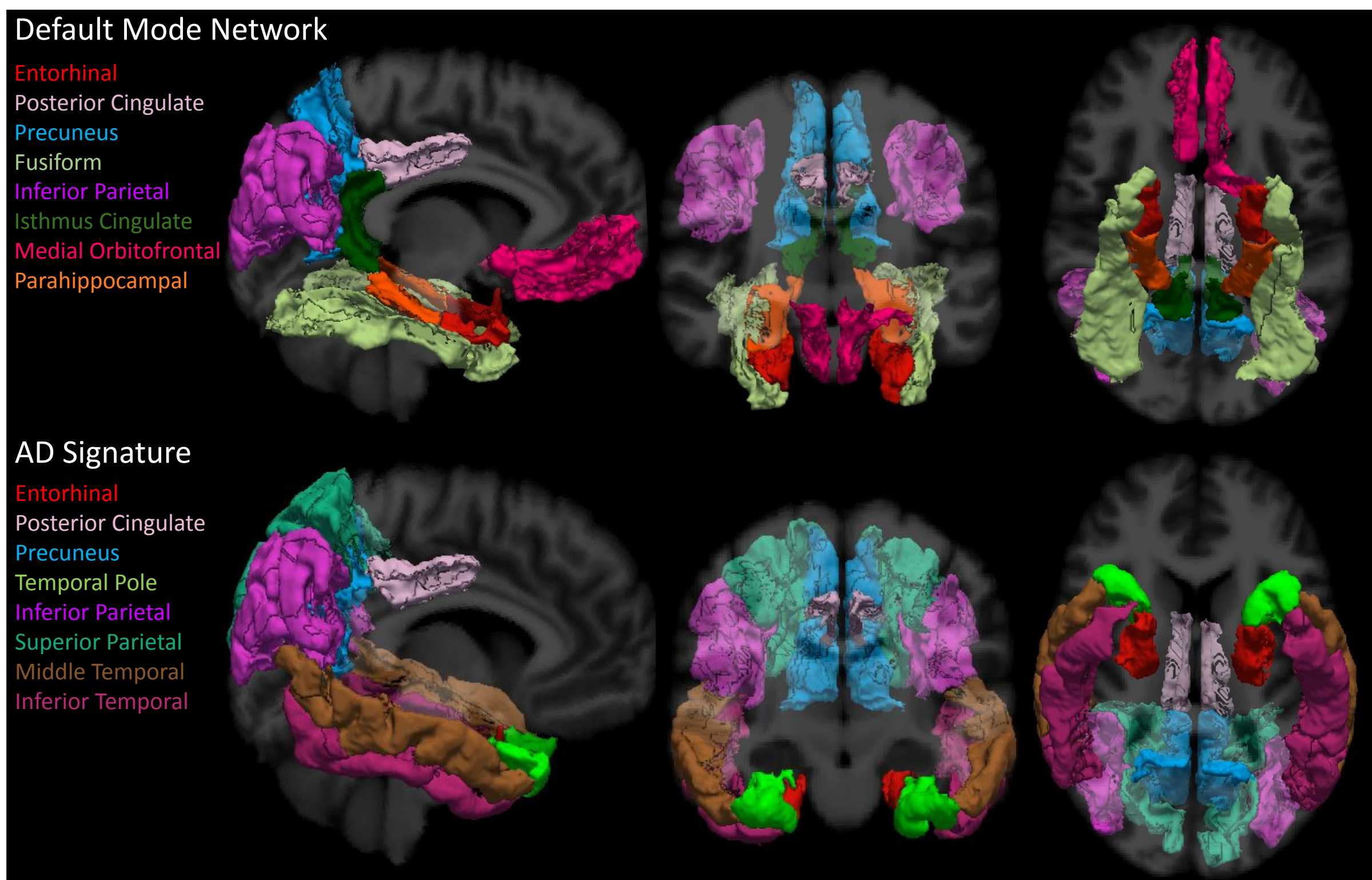
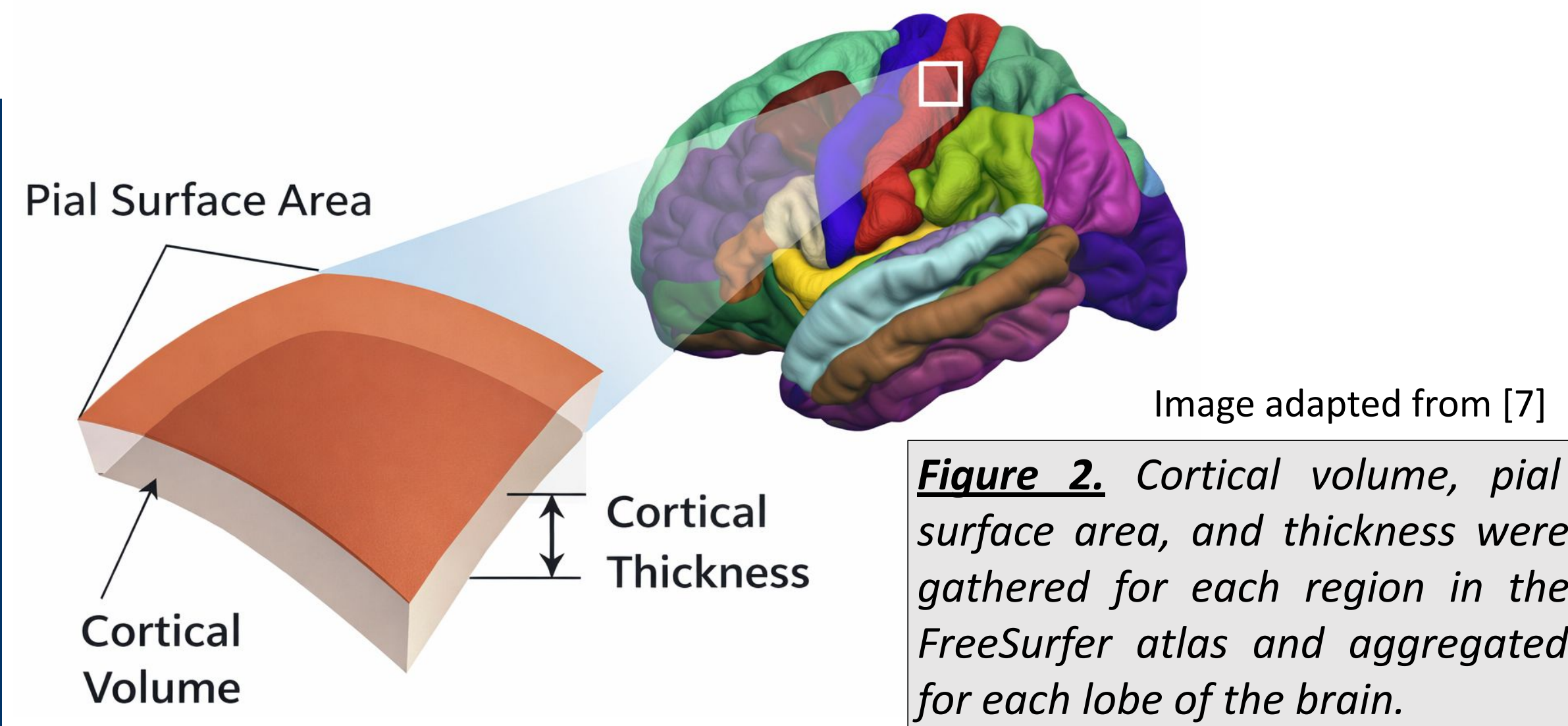


Figure 1. Cortical grey matter parcellations comprising the Default Mode Network [5] and AD Signature [6]. Three orthogonal views of cortical parcellations are shown overlaid upon a T1-weighted reference image in MNI space.



RESULTS

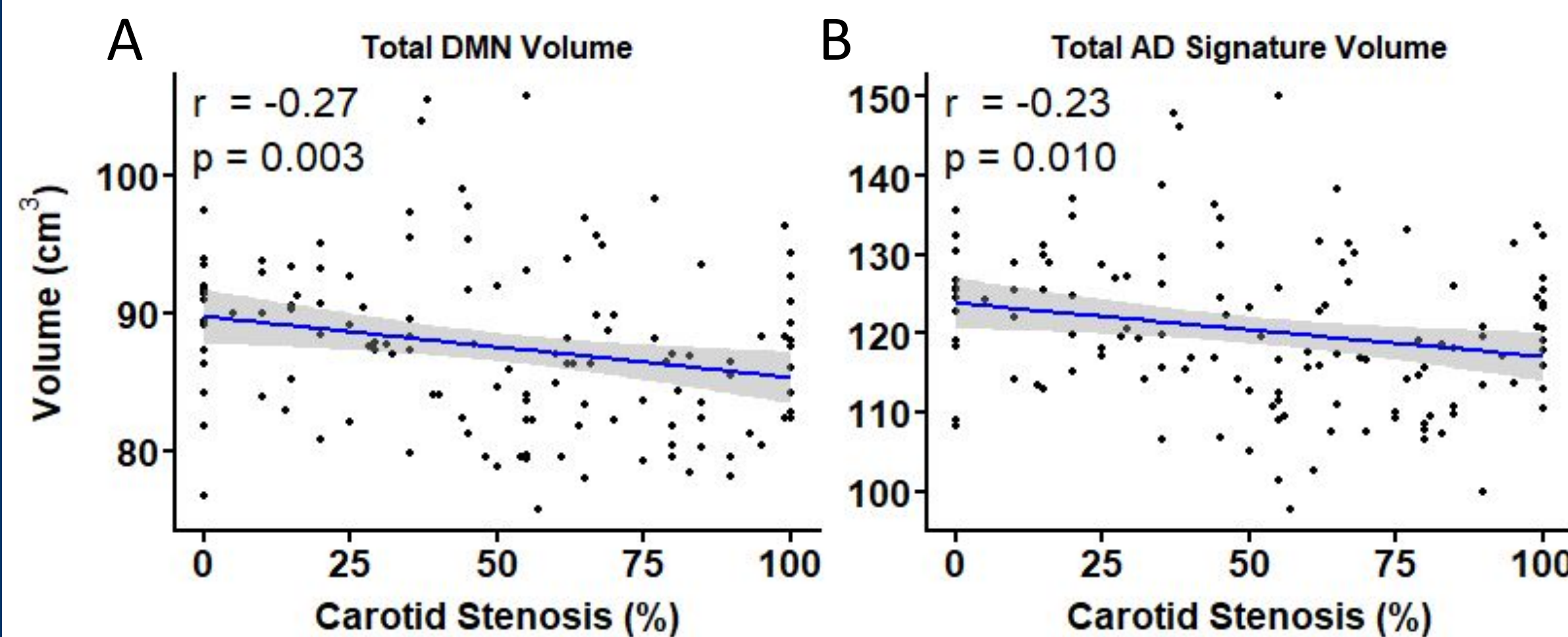


Figure 3. Total (A) Default Mode Network and (B) AD Signature cortical volumes decrease with increasing carotid stenosis severity.

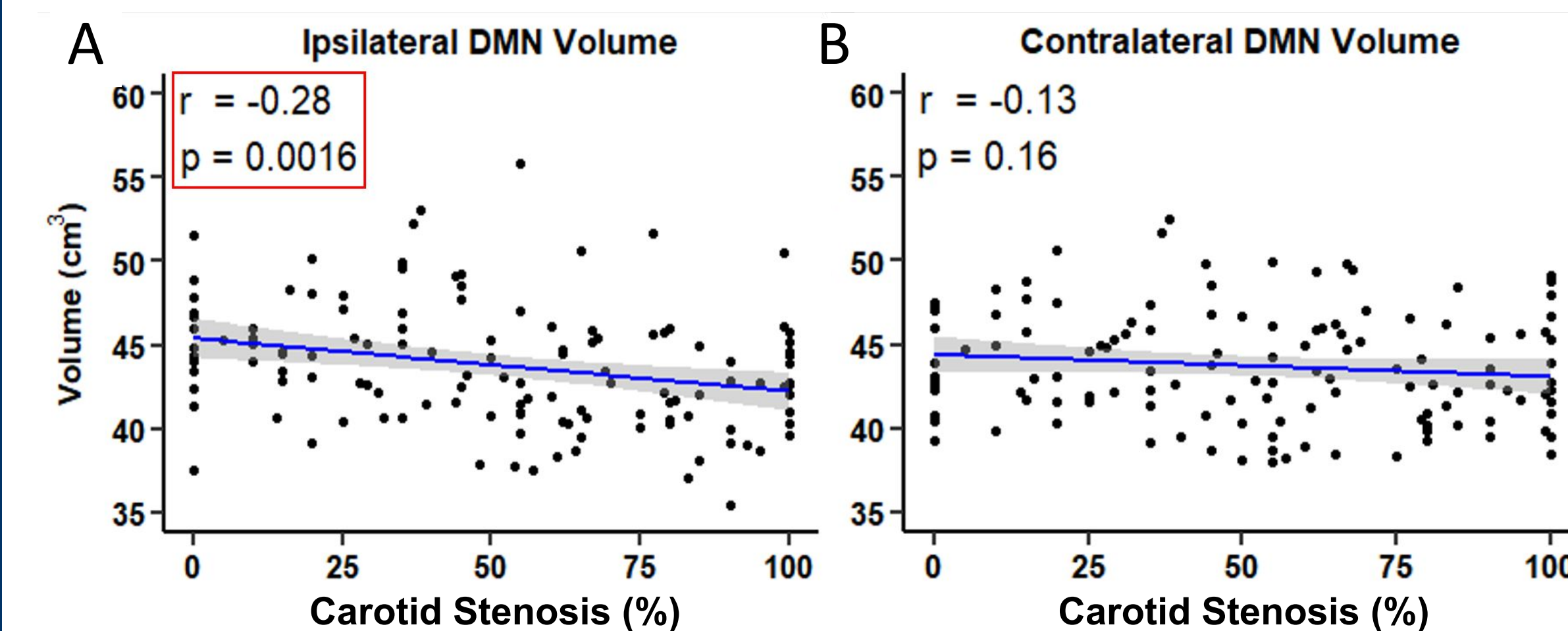


Figure 4. Volume of the DMN decreases significantly with carotid stenosis severity ipsilateral to the side of greatest disease. There is no significant relationship between volume and carotid stenosis in the contralateral hemisphere. Similar findings were observed in the AD Signature.

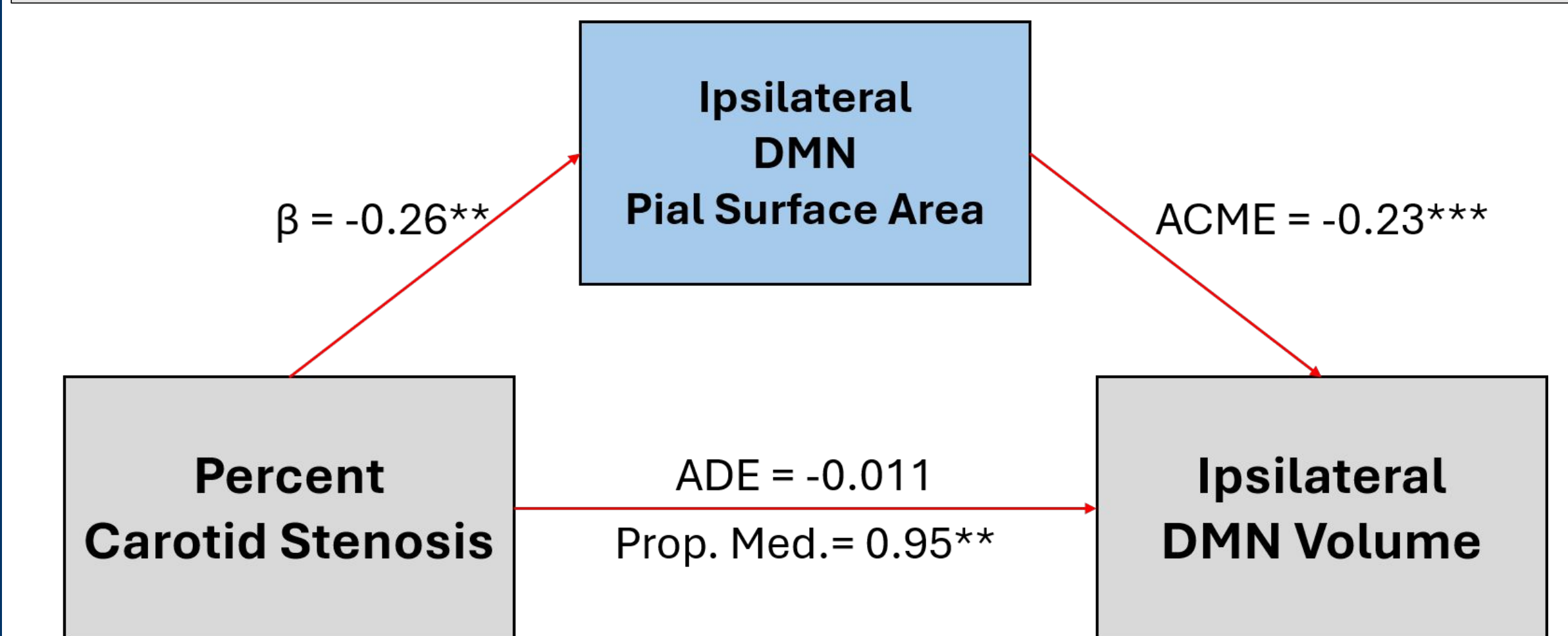


Figure 5. DMN surface area significantly mediates 95% of the stenosis-volume relationship ipsilateral to the side of stenosis. There is a small, insignificant average direct effect (ADE) between stenosis and ipsilateral DMN volume. Similar findings were observed in the AD Signature. Cortical thickness did not demonstrate significant mediation.

RESULTS

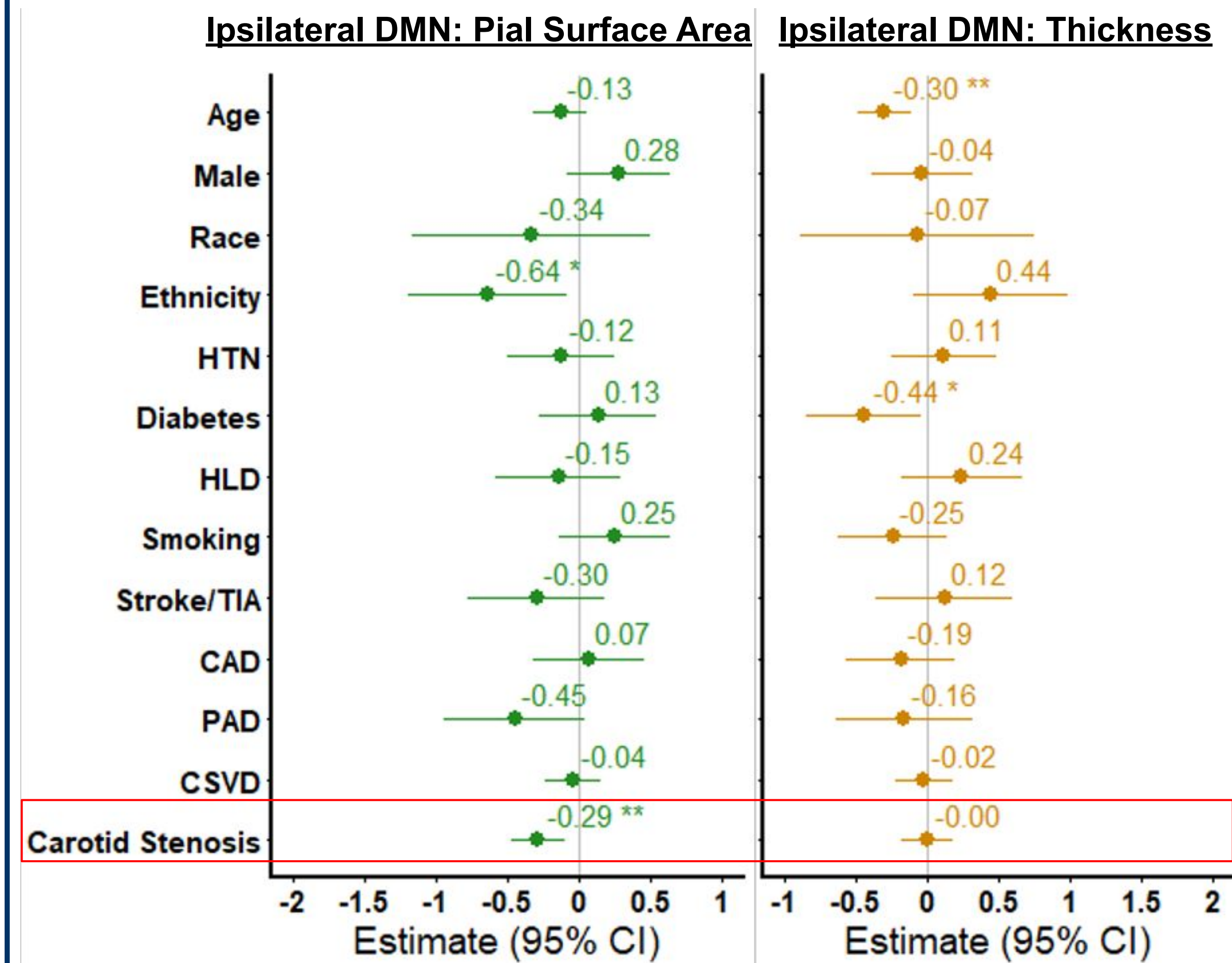


Figure 5. Multiple linear regression models demonstrate demographic and vascular risk / disease associations with ipsilateral DMN pial surface area and thickness. Carotid stenosis was independently associated with significantly lower ipsilateral DMN pial surface area, but not thickness. No significant relationship was observed for contralateral morphometrics. Abbreviations: HTN, hypertension; HLD, hyperlipidemia; TIA, transient ischemic attack; CAD, coronary artery disease; PAD, peripheral artery disease; CSVD, cerebral small-vessel disease severity.

CONCLUSIONS

- Extracranial carotid artery disease (ECAD) is associated with significant **ipsilateral brain volume loss, driven by lower surface area** in the Default Mode Network and AD Signature
- This relationship between ECAD and surface area is **independent of age, sex, and other vascular comorbidities like cSVD**
- The preferential ipsilateral association between carotid stenosis and surface area **may reflect a vascular-driven pattern of cortical vulnerability**
- **These findings suggest surface area changes may be relevant for understanding ECAD association with increased AD risk**

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