

ASSOCIATIONS BETWEEN SEX AND PERIVASCULAR SPACE VOLUMES IN THE SUNNYBROOK DEMENTIA STUDY

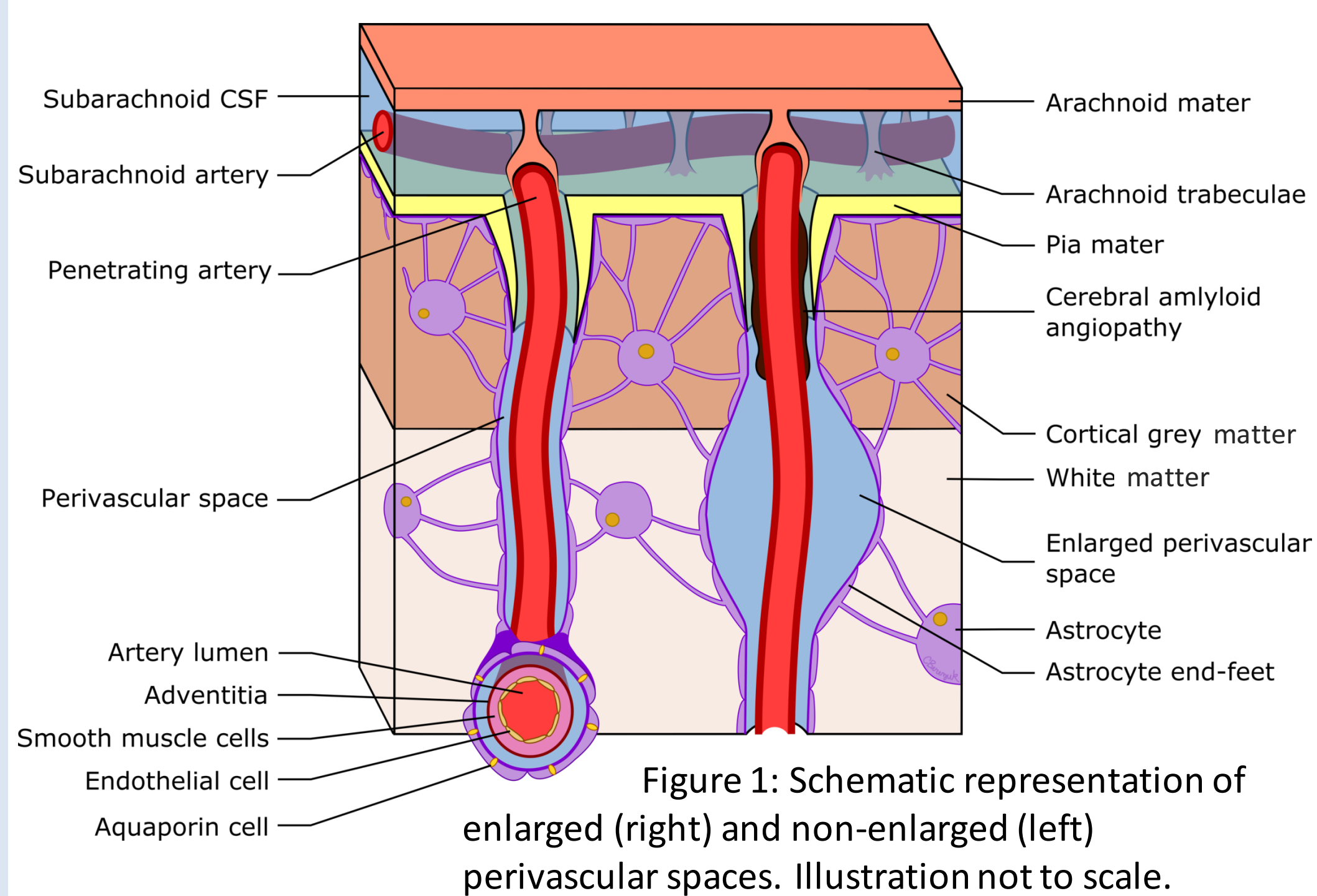
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BACKGROUND

- Perivascular spaces (PVS): the fluid-filled spaces surrounding the brain's vasculature
- May play an important role in the clearance of toxins in CSF and interstitial fluid [1].
- Enlarged PVS (ePVS) may indicate some form of small vessel disease [2]
- Possibly associated with cognitive decline [3]
- Men tend to have a greater severity of ePVS, relative to women



PURPOSE & HYPOTHESIS

Purpose: Compare ePVS volumes for men and women living with Alzheimer's disease (AD), vascular cognitive impairment (VCI), frontotemporal dementia (FTD), dementia with Lewy bodies (DLB), and healthy normal controls (NC).

Hypothesis: Based on previous research, we expect larger ePVS volumes in men, with the possibility of diagnostic differentials

- To our knowledge, ePVS sex differences in FTD and DLB have not been explored

METHODS

A modified version of Lesion Explorer (LE) [4,5] was used to automatically segment cerebrospinal fluid (CSF) intensity voxels on MRI

A trained user removed non-ePVS voxels (e.g. lacunes, subcortical hyperintensity (SH), and ventricular/sulcal CSF) from the mask

The ePVS segmentation was separated into basal ganglia (BG) and white matter (WM) regions using SABRE [4]. Manual edits were performed to improve the basal ganglia delineation.

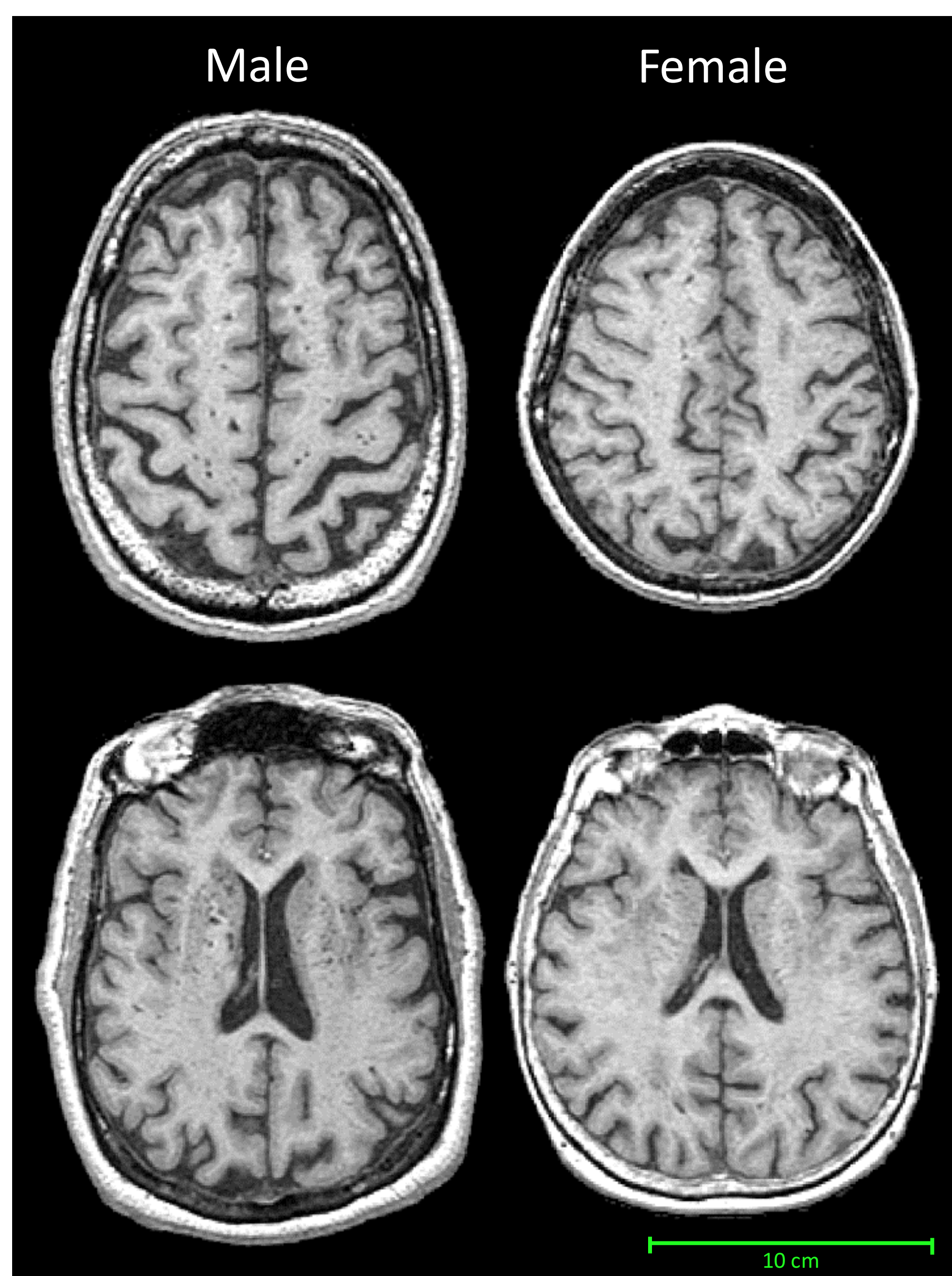


Figure 2: T1-weighted MRI of a male (left) and female (right) brain highlighting ePVS sex differences

SUBJECTS

All subjects (n=648) were taken from the Sunnybrook Dementia Study (SDS) and provided informed consent to participate

- AD (n=270)
- VCI (n=89)
- FTD (n=110)
- DLB (n=72)
- NC (n=107)

ANALYSIS

MANCOVA was used to examine sex differences for ePVS volumes

- Covariates: age, years of education (YOE), mini-mental state examination (MMSE), total intracranial capacity (TIC), brain parenchymal fraction (BPF), white matter hyperintensity (WMH) volume, and stroke volume.

Significant results were further analyzed with post hoc t-tests.

Non-normal variables were log transformed prior to analysis

RESULTS

Table 1. Multivariate test results

	F	Hypothesis df	Error df	p-value	Effect size (η^2)
Sex	0.34	3	611	0.80	-
Age	5.01	3	611	0.01	0.02
Education	0.08	3	611	0.97	-
MMSE ^a	1.69	3	611	0.17	-
TIC Volume	1.69	3	611	0.17	-
BPF Volume	1.57	3	611	0.20	-
WMH Volume	13.02	3	611	< 0.01	0.06
Stroke Volume	0.57	3	611	0.63	-
Sex*Dx	2.34	24	1839	< 0.01	0.03
Sex*Age	3.06	3	611	0.03	0.02
Sex*MMSE	0.67	3	611	0.57	-
Sex*Education	2.22	3	611	0.09	-
Sex*WMH	3.22	3	611	0.02	0.02

Data were corrected for non-normality
^a Available in 635 patients

Table 2. T-tests comparing total and regional ePVS volumes for males and females across the core SDS dementias

AD	t	df	p-value
Total ePVS	3.83	268	< 0.01
WM-ePVS	3.39	268	0.01
BG-ePVS	3.12	268	0.01
VCI			
Total ePVS	0.29	87	0.77
WM-ePVS	1.19	87	0.24
BG-ePVS	-0.38	87	0.70
FTD			
Total ePVS	-1.38	108	0.17
WM-ePVS	0.62	108	0.54
BG-ePVS	-1.19	108	0.24
DLB			
Total ePVS	1.29	70	0.20
WM-ePVS	-0.12	70	0.91
BG-ePVS	2.00	70	0.05
NC			
Total ePVS	3.82	105	< 0.01
WM-ePVS	2.93	105	0.01
BG-ePVS	2.59	105	0.01

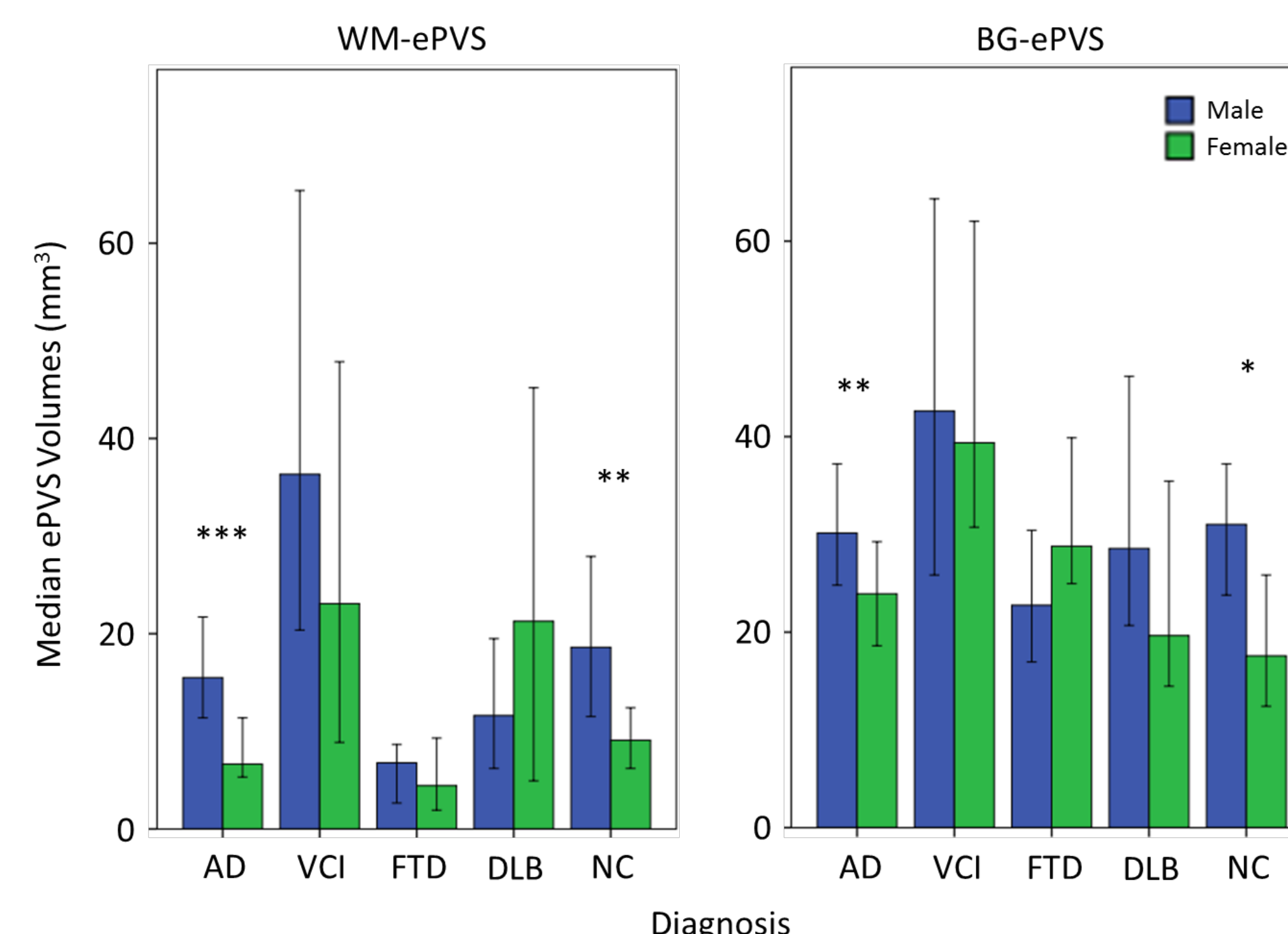


Figure 3: Median and 95% confidence interval for WM ePVS (left) and BG ePVS (right) raw volumes stratified by male (blue) and female (green)

DISCUSSION

- Existing research suggests that male sex is associated with greater severity of ePVS in:
 - Stroke patients [7]
 - Alzheimer's disease [5]
 - Normal elderly [8]
- Males appear to be at a greater risk of enlarged perivascular spaces in AD, NC and possibly in the BG of DLB patients. No sex differences were found in VCI and FTD
- Implications of these findings are limited due to uncertainty surrounding the mechanisms behind PVS enlargement
- These findings advocate for the importance of gender stratification in future ePVS research
- Future work examining sex differences in CSF clearance and sleep fragmentation may be an important avenue for exploration
- Given that ePVS have been previously associated with amyloid angiopathy, sex differences in amyloid aggregation should be explored in relation to ePVS

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