Visible perivascular spaces in elderly patients with dementia

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Background

The brain lacks conventional lymphatic vessels, but recent evidence suggests that the space surrounding the vasculature serves as a proto-lymphatic system to clear interstitial fluid and metabolic waste [1].

Called perivascular (Virchow-Robin) spaces, these tunnels are thought to act as conduits for the clearance of soluble waste and may play an important role in inflammatory and immunological responses in the brain [2].

With age, neurodegeneration, and cerebrovascular disease, these microscopic spaces are quantifiable on conventional MRI [3].

Objectives

To compare enlarged/visible perivascular space (PVS) volume burden in a sample of normal elderly participants and dementia patients enrolled in the Sunnybrook Dementia Study.

Discussion

In addition to whole brain atrophy, WMH, and left hippocampal volumes, WM-PVS may be differentially associated with different dementias with varying degrees of cerebral small vessel disease (SVD). The role of SVD and metabolic clearance through the perivascular space, especially in AD, will be explored in future work.

Although previous studies have shown PVS burden to be higher in men in both AD and normal aging [5-7], the potential factors that may explain this sex difference have yet to be fully explored.

These preliminary findings, in the context of recent work on the glymphatic system, provide an exciting new area of research that may be useful in developing novel therapeutic strategies for the treatment of neurovascular and neurodegenerative diseases such as AD and related dementias.

Results

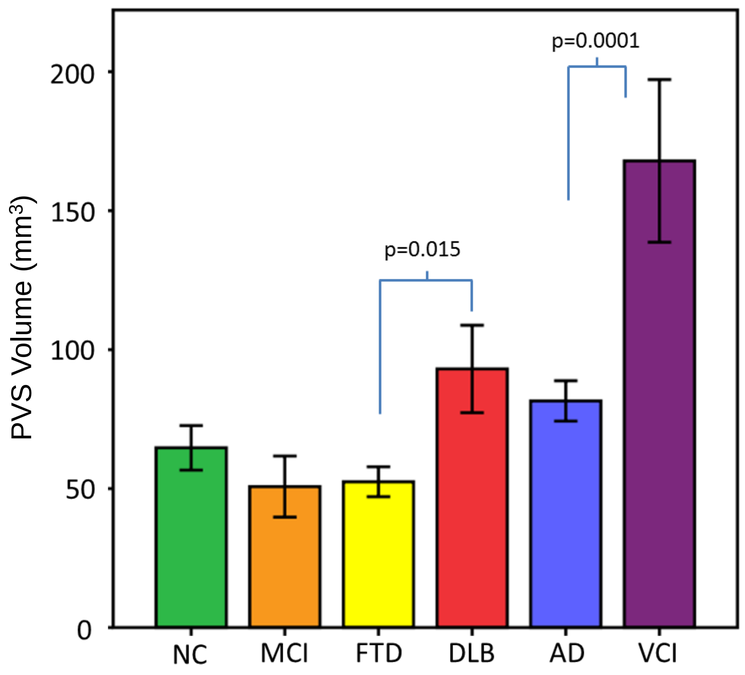

Fig. 1 Figure 5 - Mean PVS volumes across different diagnostic groups. Total PVS volumes were significantly different across groups (Kruskal-Wallis, p<0.0001). Post-hoc trend testing showed a significant linear trend across groups (p<0.001), indicating a general linear increase in PVS volumes from NC to VCI (left to right). Bonferroni corrected post-hoc tests showed a significant increase between FTD and DLB (p=0.015) and AD and VCI groups (p=0.0001), suggesting three levels of PVS burden.

Variables	β coefficient	R^2	P value	95% CI Lower	95% CI Upper	Sig
Gender	-.082	-.087	.03	-.510	-.029	n.s.
Education (years)	-.093	-.106	.01	-.072	-.011	**
Disease Severity (DRS total)	-.223	-.207	.00	-.030	-.014	***
BPF	-.138	-.108	.01	-.076	-.013	**
Ventricular CSF	.001	.001	.97	.000	.000	n.s.
Hippocampus Right	-.030	-.021	.59	-.001	.000	n.s.
Hippocampus Left	-.157	-.111	.00	-.001	.000	***
WMH	.123	.095	.02	.000	.000	*
BG-VRS	.027	.025	.52	-.002	.005	n.s.
WM-VRS	.086	.083	.04	.000	.002	*
Lacune	.044	.036	.36	.000	.001	n.s.

Table 1 Summary of regression results for demographics and imaging measures for small vessel disease and brain atrophy. DRS=dementia rating scale, BPF= brain parenchymal fraction, CSF=cerebrospinal fluid, WMH=white matter hyperintensities, BG-PVS= basal ganglia perivascular space volume, WM-PVS=white matter perivascular space volume.

Regression models revealed that education, sex, disease severity (dementia rating scale), WM-PVS, whole brain atrophy (brain parenchymal fraction), left hippocampal volume, and white matter hyperintensities (WMH), significantly accounted for the variance between the dementia groups (Table 1).

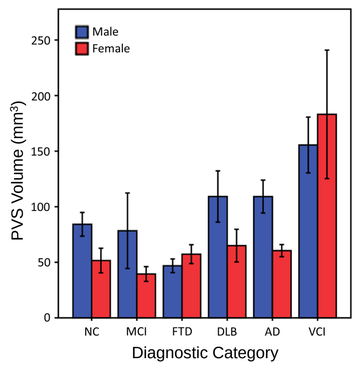

Fig. 2 When stratified by disease group, men appeared to have greater PVS volumes compared to women across all diagnostic and normal elderly groups, with the exception of FTD and VCI .

Methods

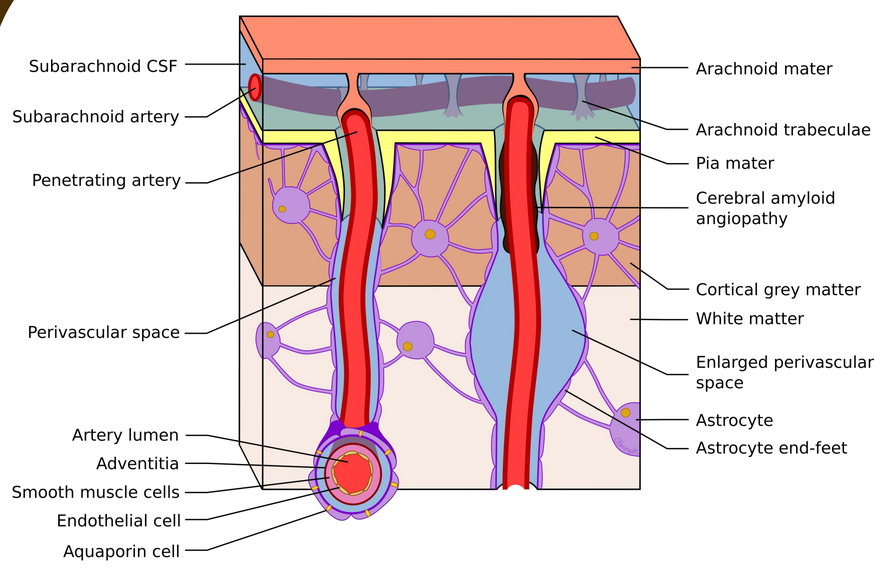

Fig. 4 Schematic representation of the brain's perivascular Virchow-Robin space and surrounding tissues. The cortical perivascular space is bounded by the adventitia of the vessel and the astrocyte end-feet, and is filled with CSF from the subarachnoid space. Beta amyloid is thought to accumulate around the blood vessel possibly resulting in perivascular blockage and enlargement of the space, as shown on the right vessel [4].

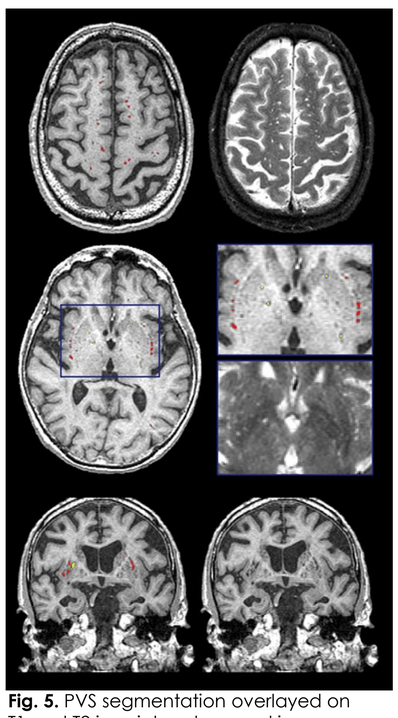

Fig. 5. PVS segmentation overlayed on T1 and T2 in axial and coronal images.

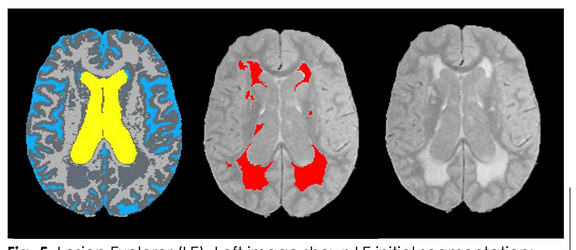

Fig. 5. Lesion Explorer (LE). Left image shows LE initial segmentation: gray matter (dark gray) and white matter (light gray), vCSF (yellow), sulcal CSF (blue). Middle image shows WMH segmentation overlayed in red. Right image shows proton density. All images have been skull stripped using the BrainSizer component of LE which includes all sCSF.

Lesion Explorer (LE)

Basic volumetrics including WMH, lacunes, vCSF, and BPF were obtained from the LE pipeline, PVS volumes were generated using modified LE [5]. Volumetrics were obtained on the following participants sampled from the Sunnybrook Dementia Study:

Normal elderly controls	(NC: n=107)
Mild cognitive impairment	(MCI: n=38)
Frontotemporal dementia	(FTD: n=110)
Dementia with Lewy bodies	(DLB: n=74)
Alzheimer's disease	(AD: n=270)
Vascular cognitive impairment	(VCI: n=89)

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