

Venular Remodeling Occurs Despite Absence of Venular Amyloid- β Deposition in Cerebral Amyloid Angiopathy

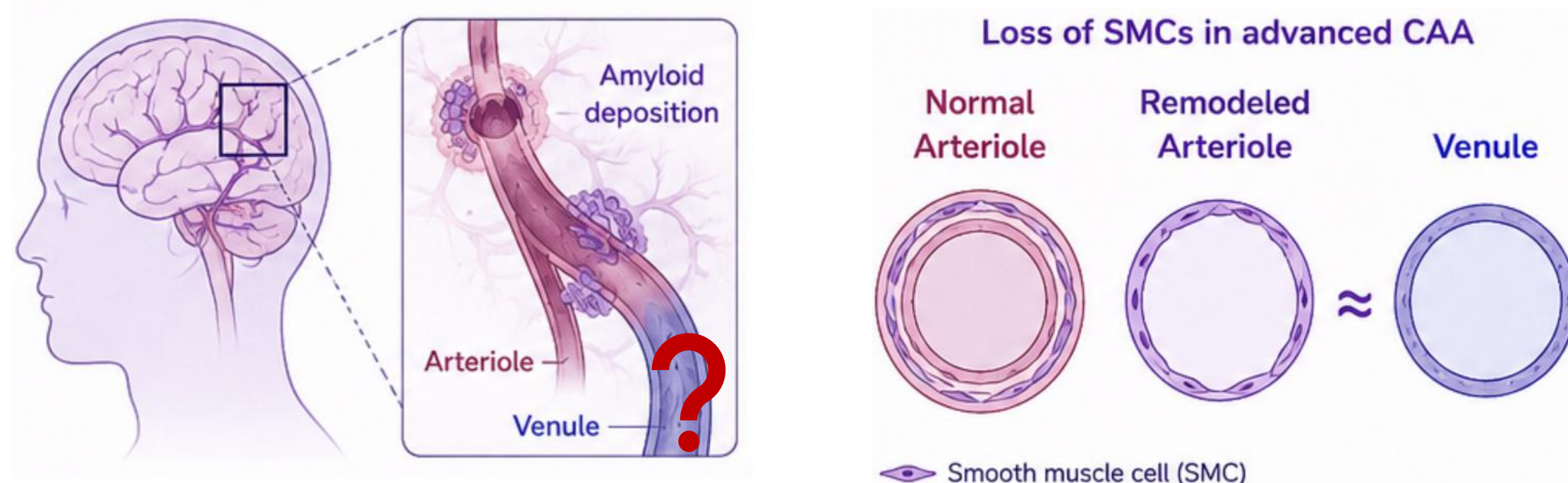
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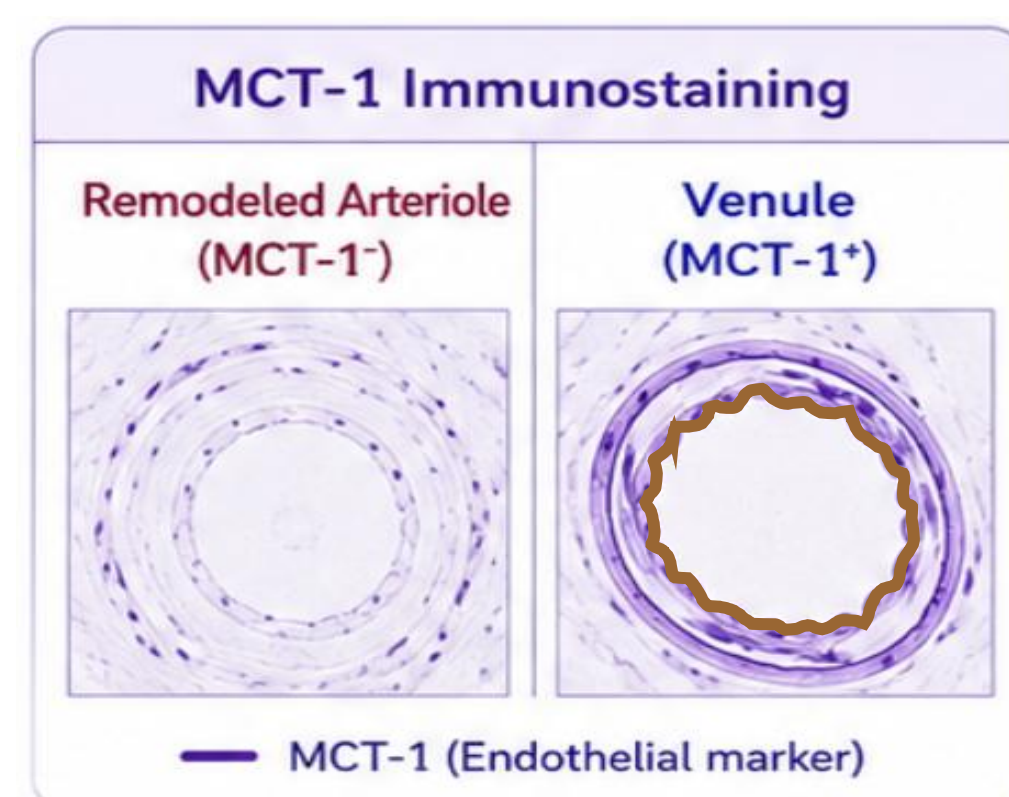
INTRODUCTION

Background: Cerebral amyloid angiopathy (CAA) is traditionally viewed as an mainly arterial disease; **the role of venules remains deeply understudied.**

The Barrier: In advanced CAA, remodeled arterioles lose their smooth muscle cells (SMCs), making them histopathologically indistinguishable from venules.



Our Solution & Aims: We leveraged **MCT-1 (monocarboxylate transporter 1)** as a reliable endothelial marker to definitively separate venules from altered arterioles, in definite, sporadic CAA human autopsies to:

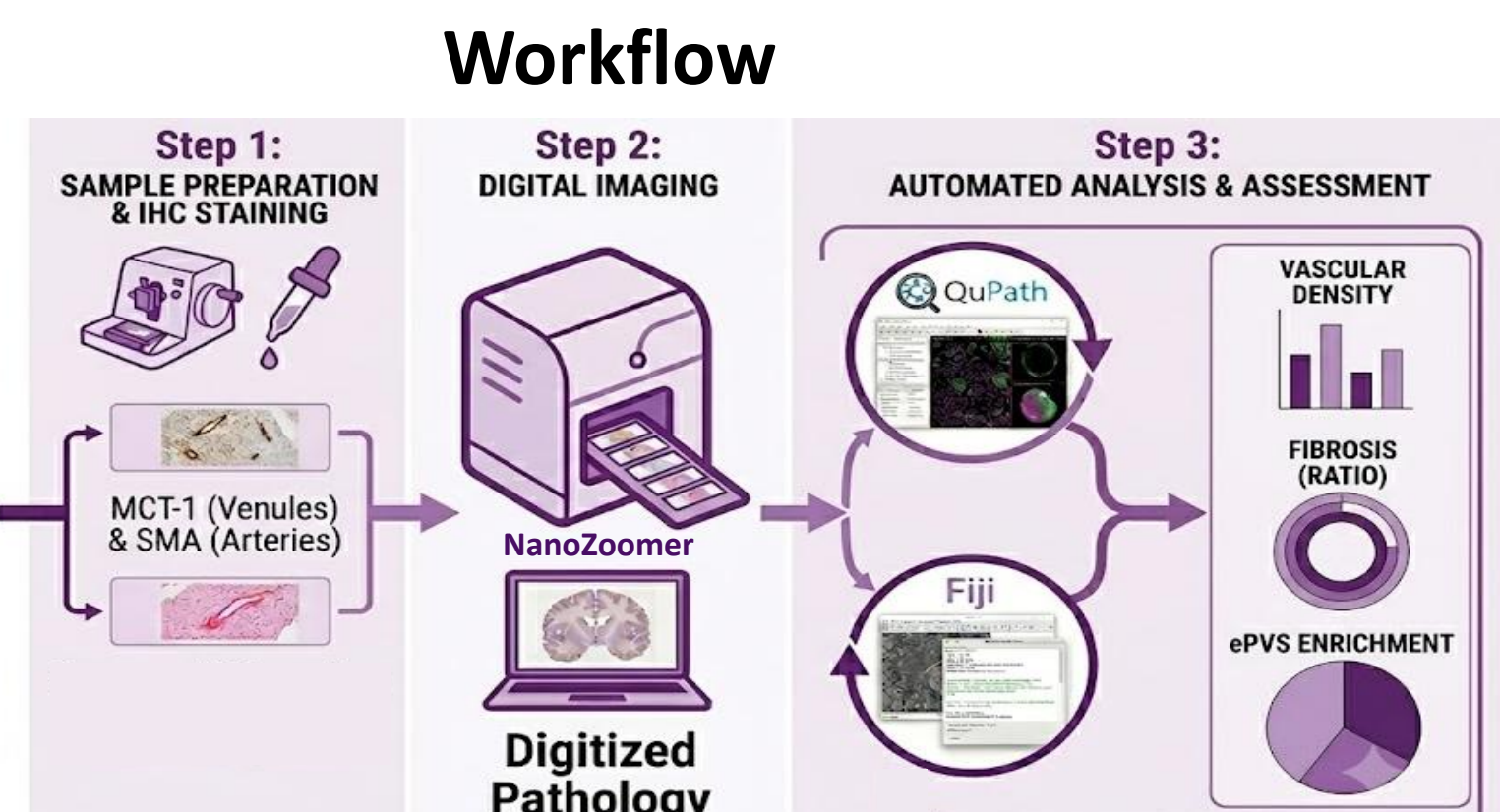


1. Assess amyloid- β (A β) deposition patterns specifically peri and within the venular wall;
2. Map & Quantify compartment-specific (cortical vs. juxtacortical WM) venular pathology, including rarefaction, fibrosis, and enlarged perivascular space (ePVS).

METHODS

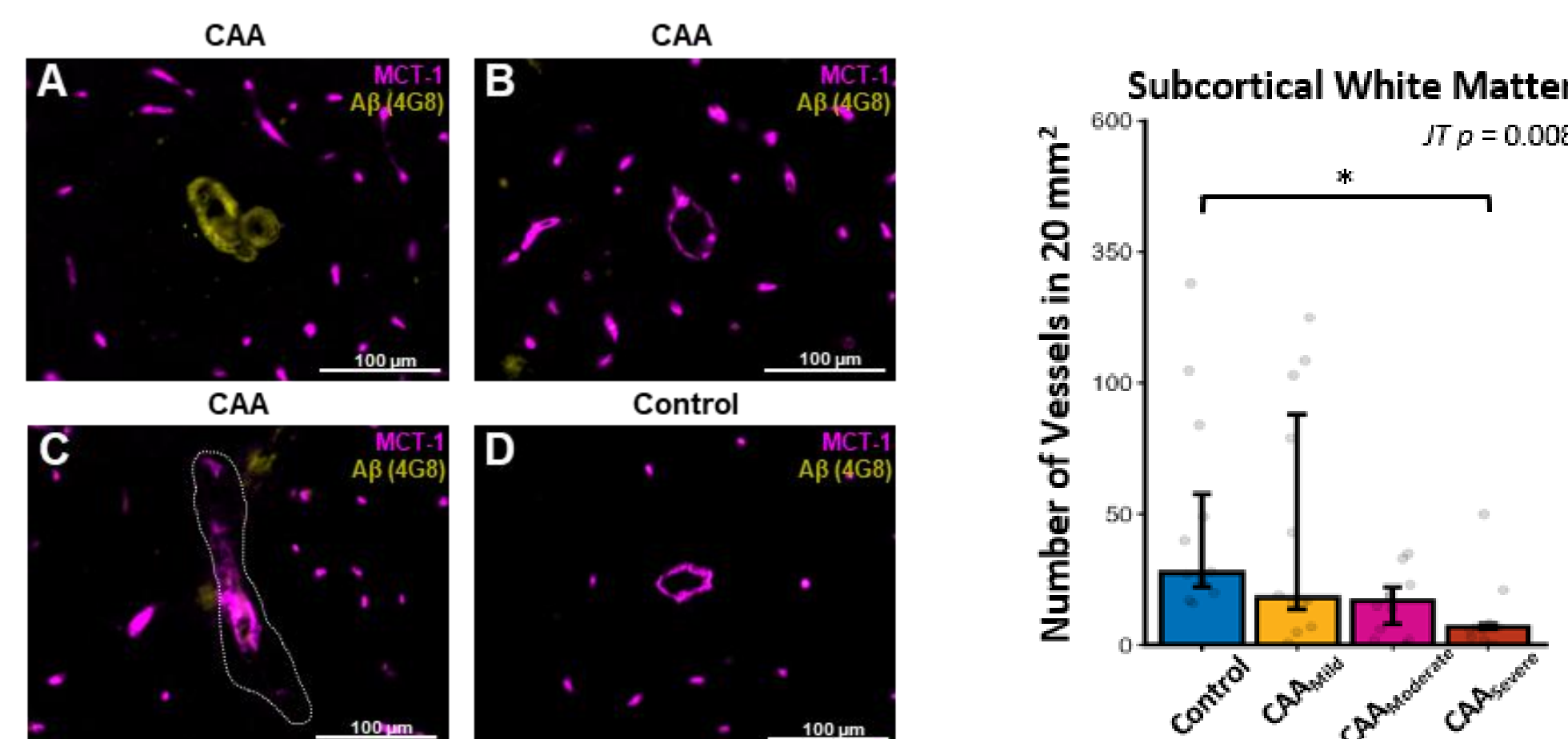
Human Tissue:
12 autopsy cases

- 9 clinically-diagnosed definite CAA
- 3 non-CAA controls

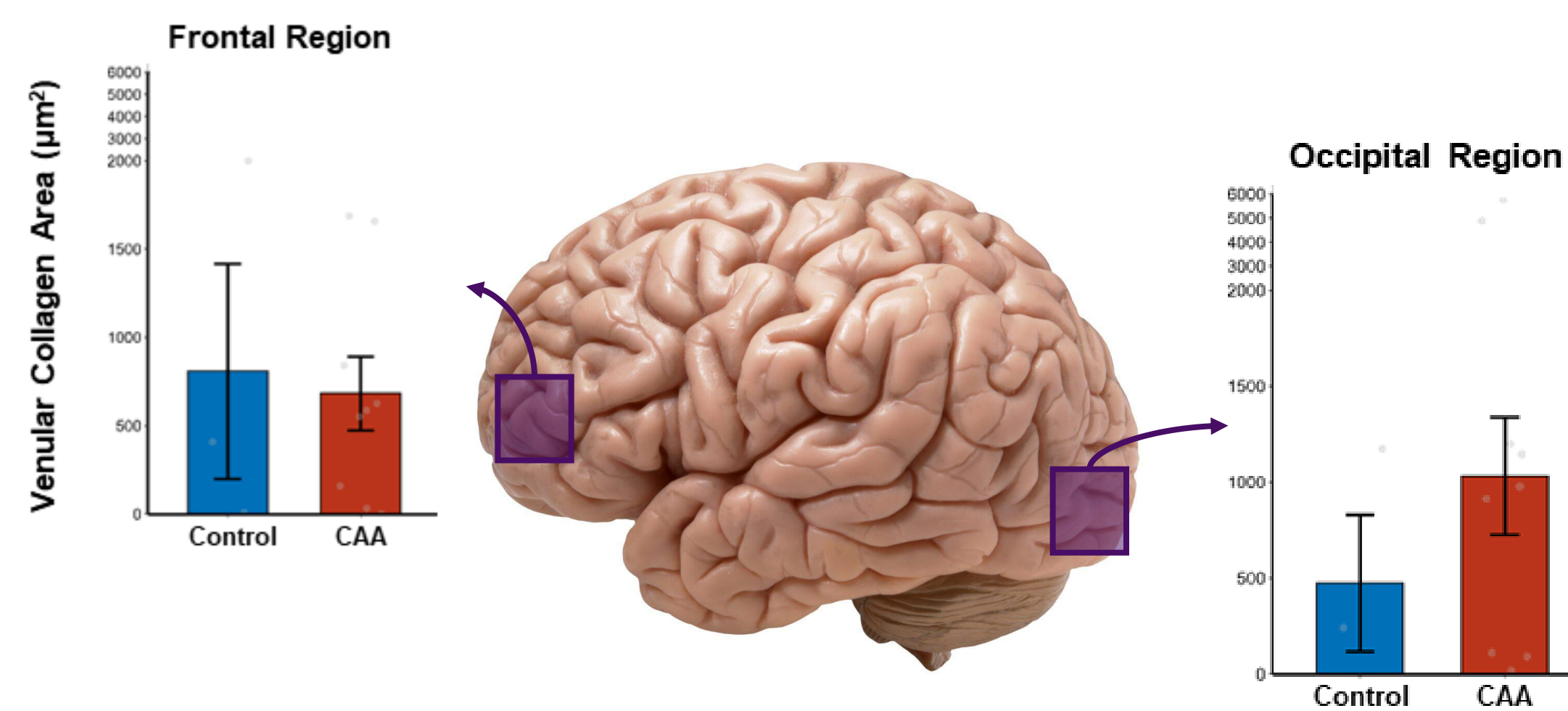


RESULTS

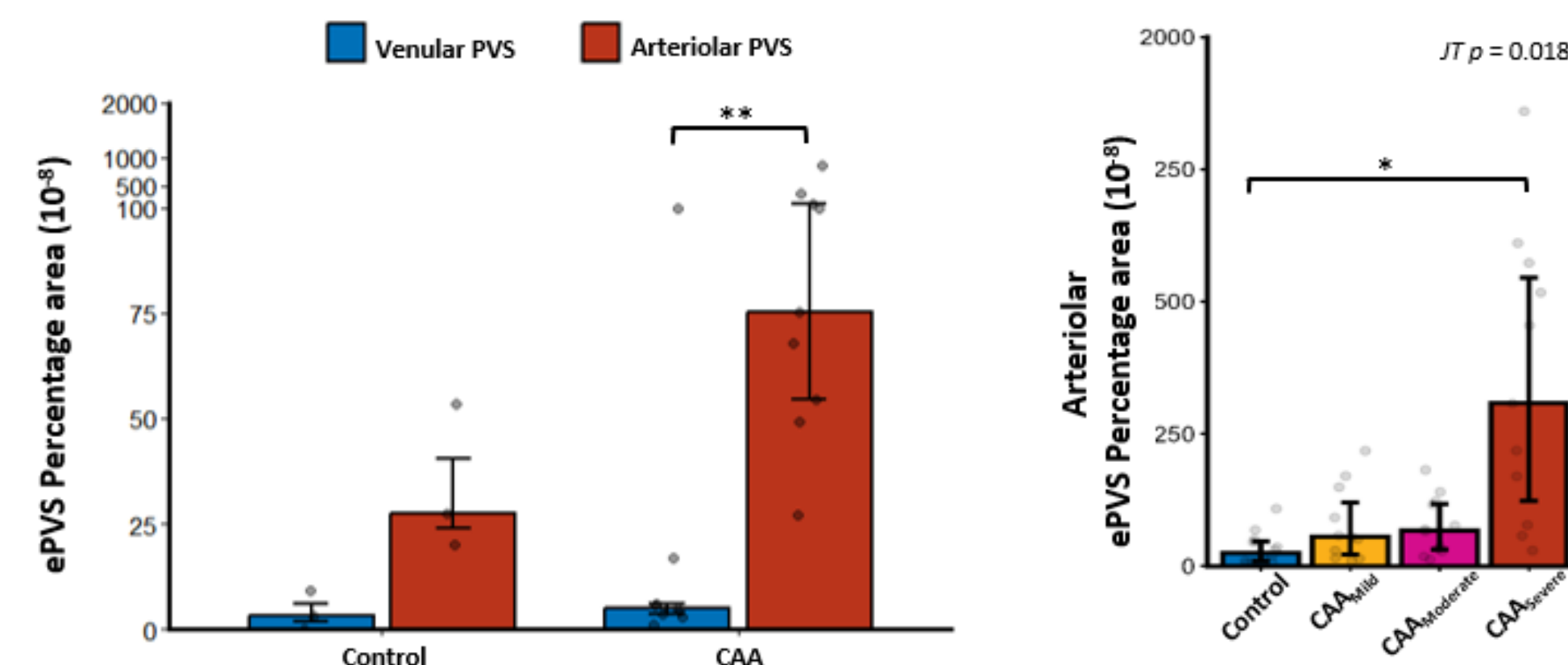
1. MCT-1-positive cortical venules showed a **100% absence** of vascular A β deposition.



2. **Venular Rarefaction:** Significantly pronounced in the subcortical white matter.
3. **Venular Fibrosis:** Prominently clustered in the occipital lobe.



4. **Arteriolar-Predominant ePVS Enlargement:** The enlargement of arteriolar ePVS tightly correlates with overall CAA severity.



CONCLUSIONS

1. In the brain parenchyma, vascular A β accumulation is exclusively arteriolar, absent in venules.
2. Venules remodel significantly with rarefaction and fibrosis in specific brain regions.
3. ePVS are predominantly arteriolar.
4. Understanding distinct pathways critical for AD clearance therapies.

Key Takeaways

1. **Arteriolar Exclusivity for A β :** A β accumulation was **absent in venules** and exclusively found in arteriolar walls in the brain parenchyma.
2. **Significant Venular Remodeling:** Despite lacking A β , venules exhibited significant **fibrosis and rarefaction** in CAA.
3. **Regional & Compartment Predominance:** Pathological changes were predominant in posterior brain regions and white matter.
4. **Predominantly Arteriolar ePVS:** ePVS burden was high around arterioles, while remaining negligible for venules.
5. **Scientific Significance:** The study demonstrates distinct microvascular pathways, providing evidence for selective arteriolar dysfunction in CAA, which may have implications for interpreting A β clearance strategies.

SCAN FOR MORE INFORMATION & CONTACT



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