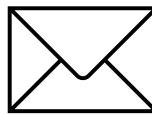


AMYLOID-VULNERABLE CORTICAL REGIONS EXHIBIT HIGHER PERFUSION IN A SUBJECTIVE COGNITIVE DECLINE COHORT.

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Cerebral perfusion may contribute to shape early amyloid deposition patterns rather than simply reflect the downstream result of neurodegeneration. Regions prone to accumulate amyloid present higher baseline perfusion and appear more vulnerable to aging and cardiovascular risk factors. These findings further highlight vascular mechanisms as potential contributor to amyloid pathology.

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	REFERENCES
Cerebrovascular dysfunction is increasingly recognized as a contributor to Alzheimer’s disease (AD) pathology, yet the relationship between perfusion and amyloid-β (Aβ) remains debated. Characterizing this association may provide insight into mechanisms underlying selective cortical susceptibility. We investigated the relationship between cerebral blood flow (CBF) and Aβ-burden in individuals with subjective cognitive decline (SCD) using arterial spin labeling (ASL) MRI and amyloid-PET.	156 participants from the FACEHBI cohort [1] underwent [¹⁸ F]-florbetaben PET and single-delay ASL-MRI. Global Aβ-burden was measured in Centiloids (CL) and used to classify participants as Aβ-negative(<12CL), gray-zone(12-30CL), or Aβ-positive(>30CL). [2] Voxelwise Z-scored SUVR maps were used to label cortical regions of interest (ROIs) with low, intermediate, and high propensity for Aβ accumulation. CBF was quantified in ExploreASL. [3]	1) REGIONAL PERFUSION FOLLOWS Aβ VULNERABILITY. Across each individual brain, CBF differed significantly between Aβ- propensity regions with a stepwise increase from low- to high-vulnerability areas (intermediate vs low β=14.59, p<0.001; high vs intermediate β=7.12, p<0.001) 2) AGING AND LIFESTYLE PREFERENTIALLY AFFECT CBF IN Aβ-VULNERABLE REGIONS. 3) CBF–Aβ COUPLING WEAKENS WITH Aβ BURDEN. Gray-zone participants maintained similar positive CBF–SUVR slopes (β=16.06, p=0.004) while Positive individuals showed significant attenuation of this relationship (β=-12.95, p=0.001).	The associative cortices of the default mode network, largely overlapping with ROIs of high propensity to accumulate Aβ, represent metabolically demanding territories with higher perfusion. CBF in these areas is particularly vulnerable to aging and lifestyle-related cardiovascular burden. The observed attenuation of CBF–Aβ positive association in Positive subjects supports the presence of evolving neurovascular dysfunction. Altogether, these results reinforce the concept that vascular mechanisms play an active role in early AD and may contribute to shaping the anatomical pattern of early amyloid accumulation.	[1] Rodriguez-Gomez O et al. FACEHBI: A prospective study of risk factors, biomarkers and cognition in a cohort of individuals with subjective cognitive decline. Study rationale and research protocols. J Prev Alzheimers Dis 2017;4:100–8. DOI: 10.14283/jpad.2016.122 . [2] Collij LE et al. Centiloid recommendations for clinical context-of-use from the AMYPAD consortium. Alzheimers Dement 2024;20:9037–48. DOI: 10.1002/alz.14336 . [3] Mutsaerts HJMM et al. ExploreASL: An image processing pipeline for multi-center ASL perfusion MRI studies. Neuroimage 2020;219:117031. DOI: 10.1016/j.neuroimage.2020.117031
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