

Genetically Predicted Lung Function Is Associated With Dementia Risk Through Glymphatic-related Imaging Markers

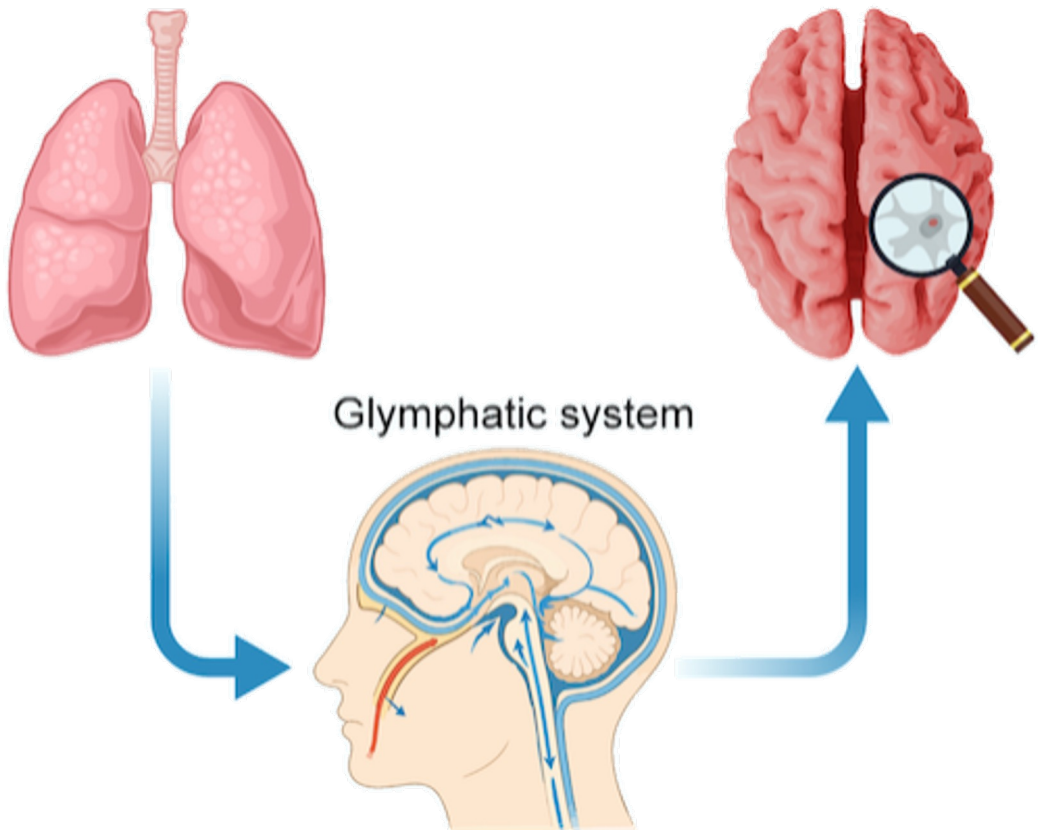
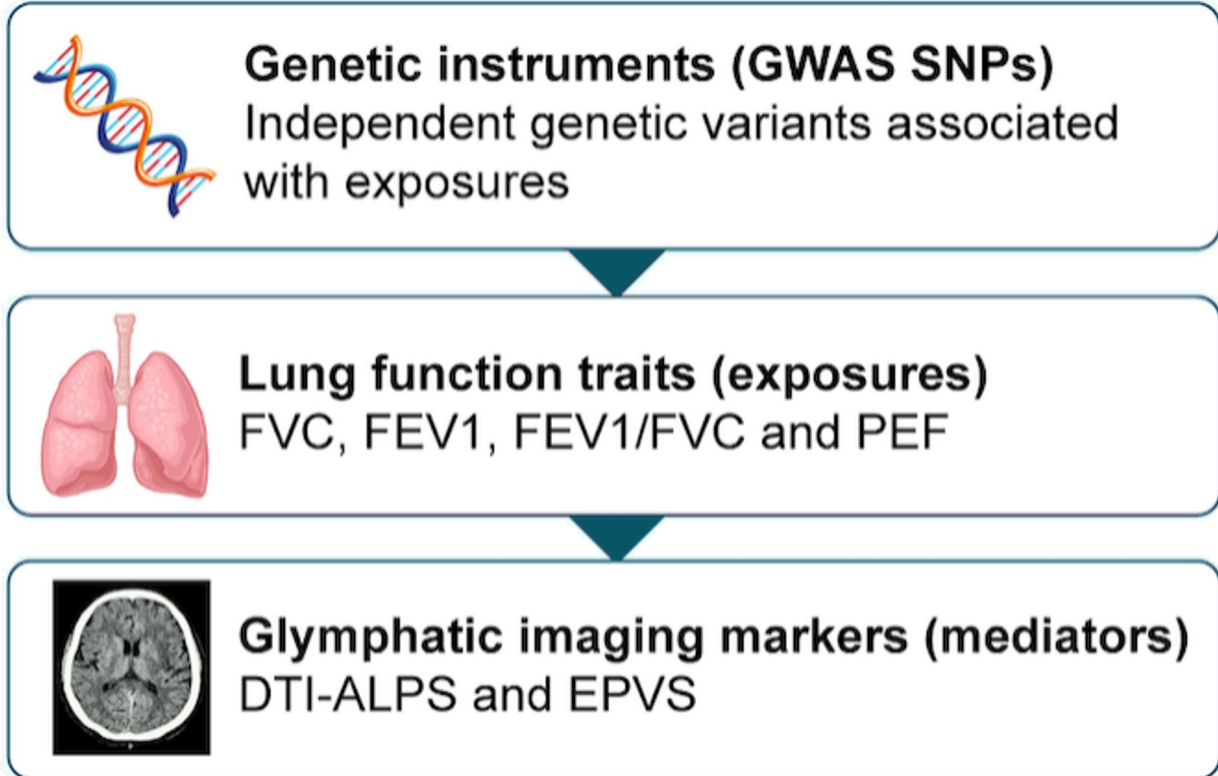
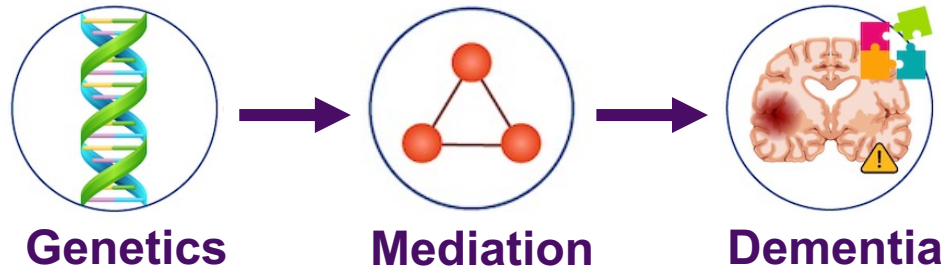
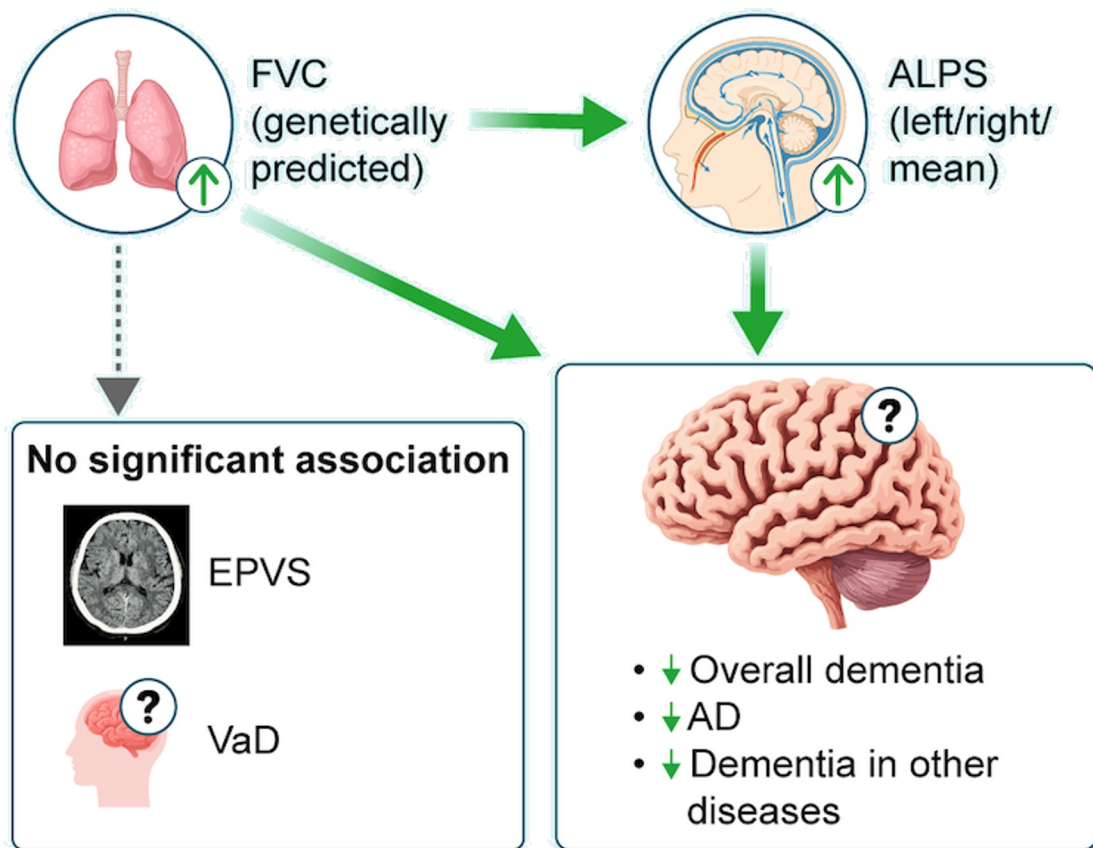
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- Higher genetically predicted FVC is associated with better glymphatic function;
- Higher ALPS indices are associated with lower risks of dementia, particularly AD and dementia in other diseases;
- DTI-ALPS may represent a promising imaging biomarker linking pulmonary health and brain aging.

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	REFERENCES
• Reduced lung function has been associated with dementia in observational studies. • Glymphatic system plays a key role in brain waste clearance and may contribute to neurodegeneration. • Whether impaired pulmonary function influences dementia risk through glymphatic dysfunction remains unknown. 	• Two-sample Mendelian randomization analysis using GWAS summary statistics. • Exposure: Lung function (FVC, FEV1, PEF, FEV1/FVC). • Mediators: Glymphatic-related imaging markers (DTI-ALPS and EPVS). • Outcomes: Overall dementia, and subtypes of dementia • Analysis: Univariable MR and two-step mediation. 	• Higher genetically predicted FVC was associated with higher mean ALPS index ($\beta=0.09$, $P=0.003$), but not with EPVS. • Higher ALPS indices were associated with lower risks of overall dementia, AD, and dementia in other diseases ($OR=0.58$, $P=0.013$), but not VaD. • Higher FVC was associated with a reduced risk of dementia in other diseases ($OR=0.72$, $P=0.017$). • Mediation analysis suggested a possible pathway via ALPS (mediation proportion $\approx 14\text{--}16\%$; $P>0.05$). 	• Preserved pulmonary function is genetically associated with more favorable glymphatic-related imaging markers. • DTI-ALPS, rather than EPVS, showed consistent associations with both lung function and dementia outcomes. • These findings support a potential lung–brain axis involving glymphatic function that warrants further investigation. 	Xiao T, et al. Lung Function Impairment and the Risk of Incident Dementia: The Rotterdam Study. J Alzheimers Dis, 2021, 82(2): 621-30; Grande G, et al. Lung function in relation to brain aging and cognitive transitions in older adults: A population-based cohort study. Alzheimers Dement, 2024, 20(8): 5662-73. Zhou L, et al. Association of impaired lung function with dementia, and brain magnetic resonance imaging indices: a large population-based longitudinal study. Age Ageing, 2022, 51(11). CONTACT Correspondence: Jie Zhang, zhangjie91@zju.edu.cn Zhejiang Provincial People’s Hospital Hangzhou, 310014  ALZHEIMER'S ASSOCIATION AAIC 26