

Peripheral Inflammation, Choroid Plexus, and Alzheimer’s Disease Progression

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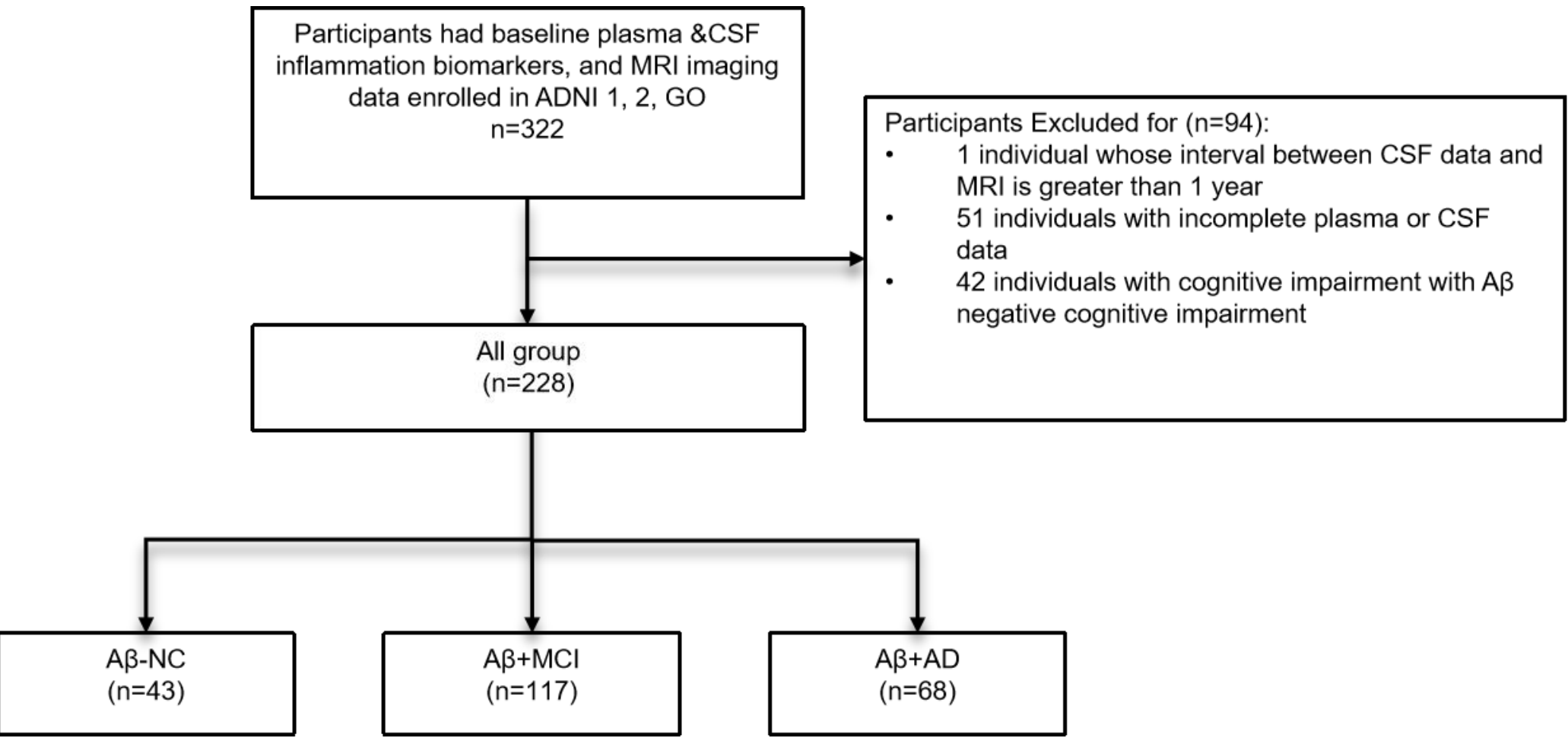
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INTRODUCTION

Choroid plexus (CP) dysfunction has been implicated in the pathogenesis of Alzheimer’s disease (AD). However, whether CP dysfunction mediates the peripheral inflammation and its impact on AD pathologies and cognitive decline within the AD continuum remains unknown.

METHODS

From the Alzheimer’s Disease Neuroimaging Initiative (ADNI) database, we included participants among cognitively normal (CN), mild cognitive impairment (MCI) and AD dementia. All participants had 26 plasma and 10 cerebrospinal fluid (CSF) inflammatory factors, CSF AD biomarkers (Aβ42, T-Tau and P-Tau181) and magnetic resonance imaging (MRI) data. CP volumes were quantified using FreeSurfer version 6.0. Multivariable linear regression models were employed to assess the correlation among inflammatory factors, AD biomarkers and CP volume. Additionally, structural equation modeling (SEM) was utilized to investigate the interactions among inflammatory factors, CP volume, AD biomarkers, and cognitive declines.



RESULTS

Characteristic	All group (n=228)	Aβ-CN (n=43)	Aβ+MCI (n=117)	Aβ+AD (n=68)	p value
Age (year)	74.9 ± 7.2	75.7 ± 6.0	74.8 ± 7.2	74.5 ± 7.8	0.204
sex					<0.001***
Male	94(41.2%)	20(46.5%)	43(36.8%)	31(45.6%)	
Female	134(58.8%)	23(53.5%)	74(63.2%)	37(54.4%)	
APOE ε4	133(58.3%)	5(11.6%)	73(62.4%)	55(80.9%)	<0.001***
History of Cardiovascular Disease	33(14.5%)	5(11.6%)	18(15.4%)	10(14.7%)	0.510
ICV (mm³)	1555207.5 ± 178664.4	1508204.7 ± 168187.1	1567477.6 ± 171310.8	1563818.2 ± 194554.9	0.159
LV Volume (mm³)	44308.0 ± 22969.5	32051.0 ± 18042.5	45004.4 ± 21933.3	50680.4 ± 24724.9	<0.001***
HP Volume (mm³)	6318.2 ± 1011.5	7215.5 ± 816.4	6250.9 ± 882.8	5879.9 ± 993.2	<0.001***
CP/ICV(%)	0.12% ± 0.03%	0.11% ± 0.03%	0.12% ± 0.03%	0.12% ± 0.03%	0.076
CDR-SB	0.5(0-1)	0	2(1-3)	4.5(3.5-5.875)	<0.001***
MMSE	26(24-29)	28(27-30)	27(25-28)	23 (21-25)	<0.001***

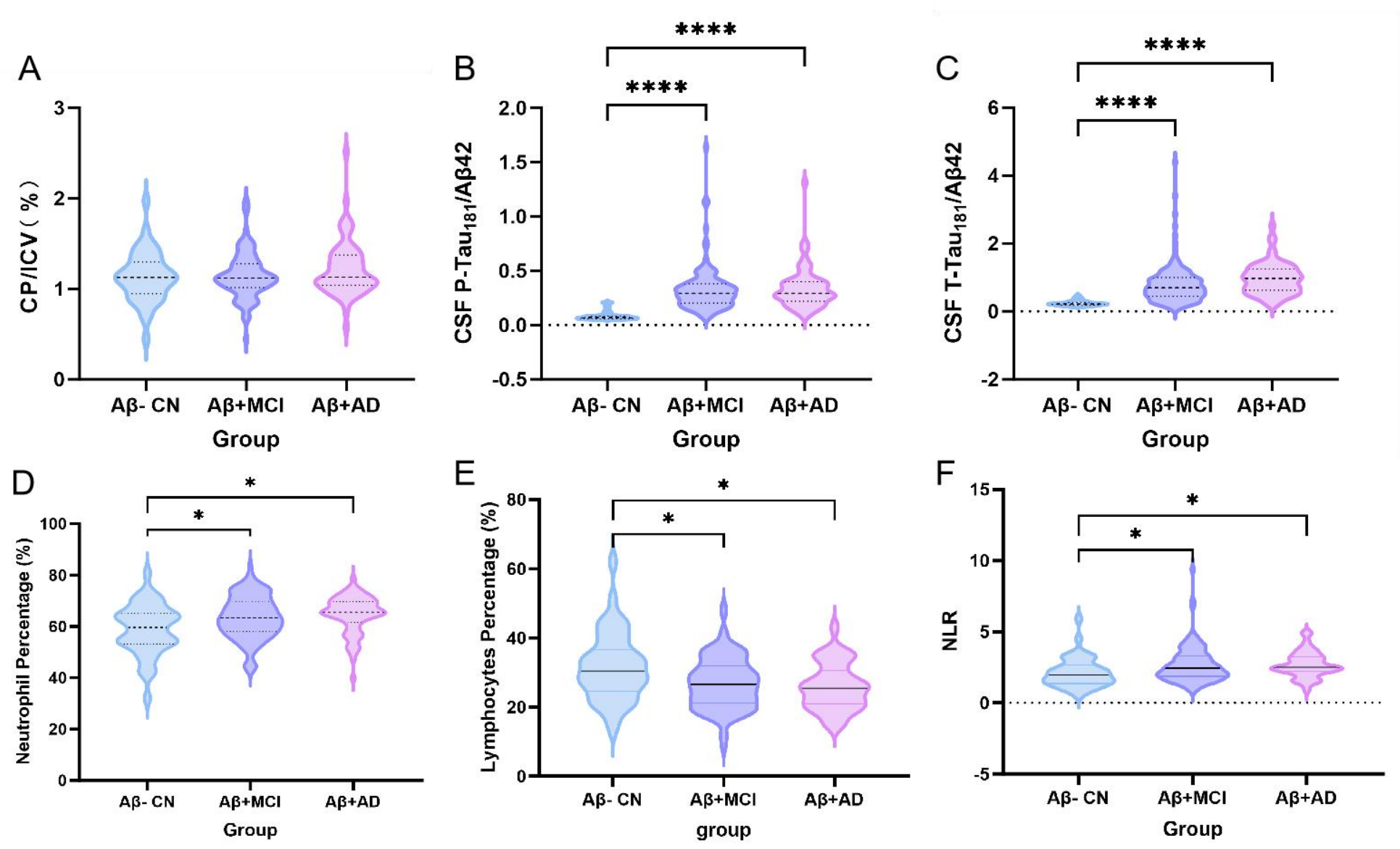


Fig2. Group comparison of plasma inflammatory factors, CSF AD biomarkers, CP volume. We observed significant differences in peripheral inflammatory factors (p < 0.05) and a trend towards increased CP volume (p = 0.076) among Aβ- CN, Aβ+ MCI and Aβ+ AD groups.

RESULTS

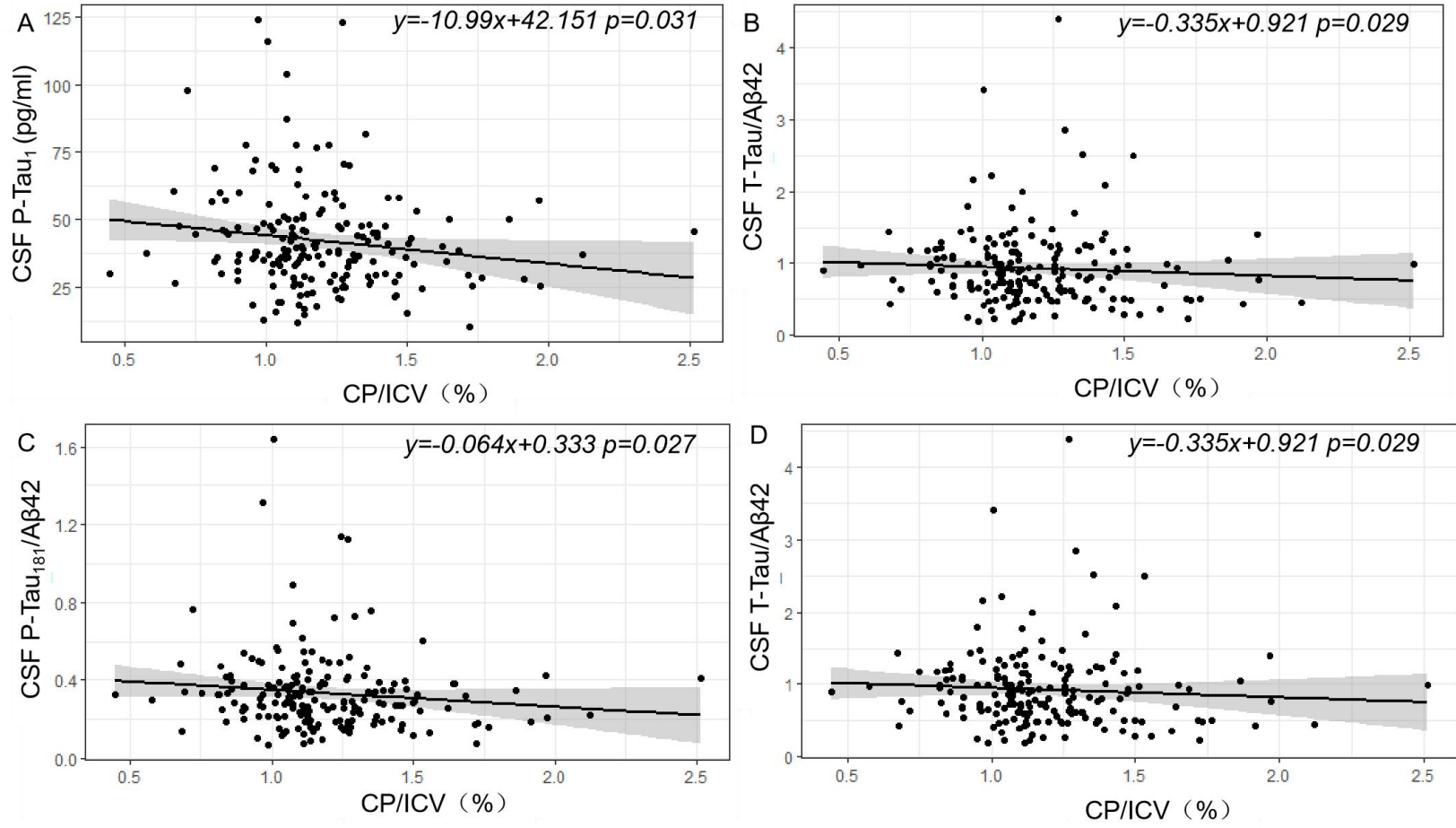


Fig3. Correlation between CP volume and CSF biomarkers in Aβ+ group. The larger CP volume was associated with higher AD pathological burden in the Aβ+ group after adjusting for age, sex, APOE ε4 carriership and ICV (p < 0.05). CP volume was associated with both plasma and CSF inflammatory factors (p < 0.05).

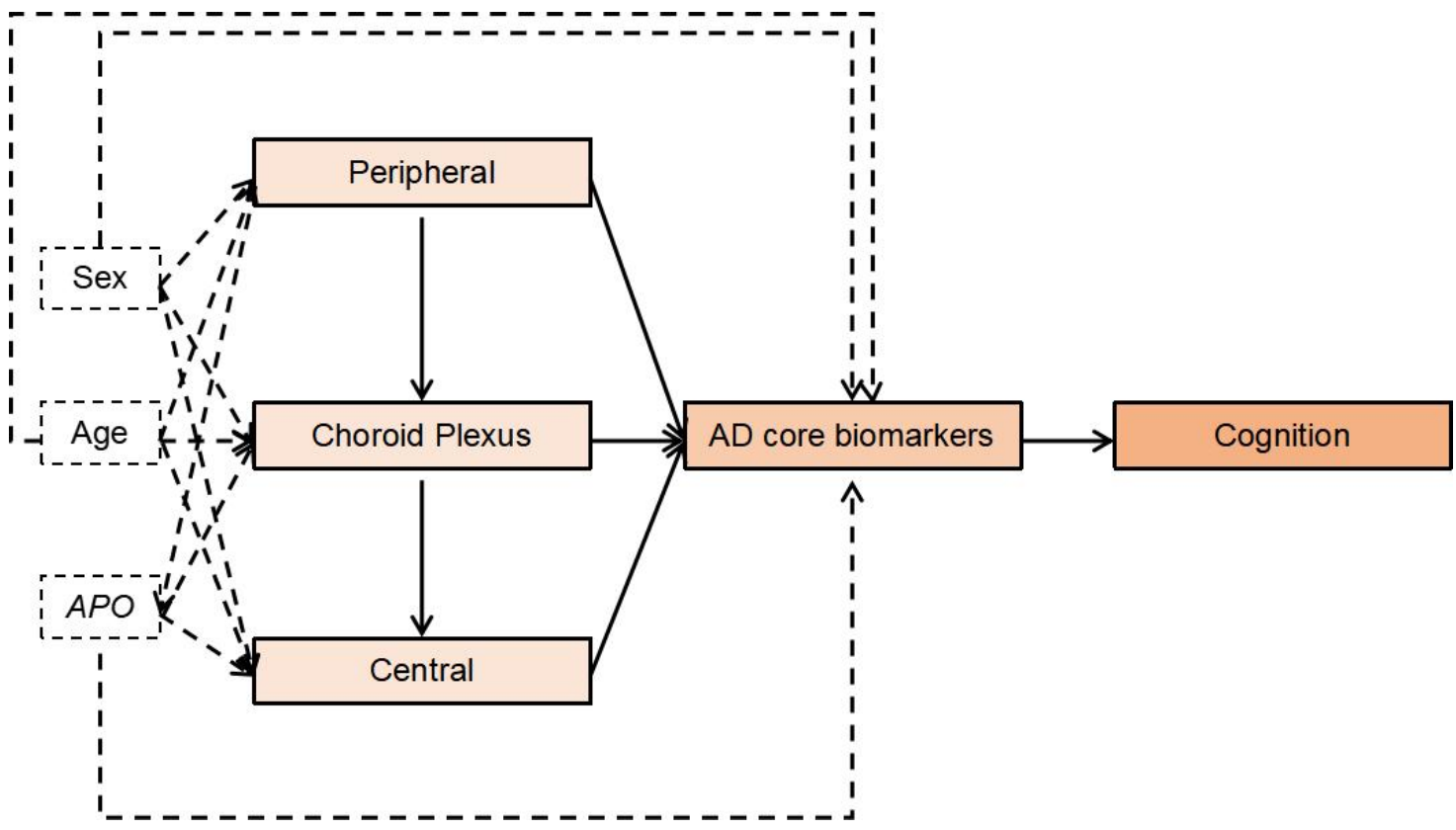


Fig4. Path analysis showing the impact of CP, peripheral inflammation, and central inflammation on AD core biomarkers and cognition. CP volume mediated the relationship between peripheral inflammation and AD pathologies using SEM.

CONCLUSION

Our study demonstrated that CP volume mediates the effects of peripheral inflammation on central inflammation, which could increase the AD pathological burden and lead to cognitive dysfunction.