

Title: APOE ε4 May Modify Associations between Plasma Alzheimer's Disease Biomarkers and Retinal Imaging Metrics in Cognitively Normal Adults



Presenter:
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Background

- Apolipoprotein E (APOE) ε4 allele is the single greatest risk factor for sporadic Alzheimer's Disease (AD)
- Plasma biomarkers are an emerging AD diagnostic modality
- Retinal imaging offers a noninvasive window into early neurodegenerative changes
- Limited data on how plasma AD biomarkers correlate with retinal imaging
- +how relationship differs based on APOE ε4 carrier status

Methods

- Subjects:** cognitively normal APOE ε4 carriers and noncarriers
 - Retinal imaging within 1 year of plasma sampling
 - Exclusion criteria: diabetes, glaucoma, vitreoretinal pathology, VA<20/40
- Imaging:** OCT and OCTA (Zeiss Cirrus HD-5000 AngioPlex)
- Statistics:** linear mixed-effects models adjusted for age, sex, treated hypertension, years of education
 - Interactions by APOE ε4 status assessed

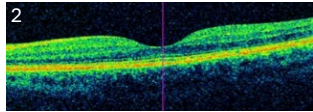


Figure 2. Sample OCT image used to measure CST, GCIP, RNFL thickness

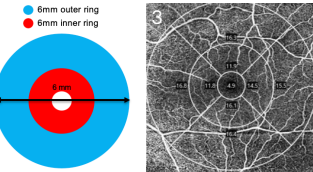
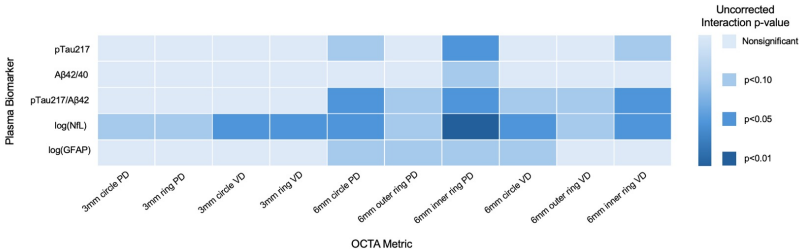


Figure 3. Sample 6x6mm OCTA image used to measure PD, VD

APOE carrier status may modify relationships between plasma Alzheimer's disease biomarkers and retinal OCT/OCTA metrics in cognitively normal adults

Figure 1. Heatmap of plasma biomarker-OCTA associations with interaction by APOE carrier status



Results & Discussion

Table 1. Demographic Characteristics

Group		ε4 Noncarriers	ε4 Carriers	P-value
N (patients)		N = 24 (46 eyes)	N = 20 (37 eyes)	
Age, mean (SD)		65.7 (7.5)	61.9 (8.1)	0.12
Female sex, N (%)		16 (66.7)	14 (70)	1.00
Race, N (%)	White	20 (83.3)	19 (100)	0.18
	Black	3 (12.5)	0 (0)	
	Hispanic	1 (4.2)	0 (0)	
Hypertension, N (%)		5 (21.7)	1 (5.3)	0.28
MMSE, mean (SD)		29.42 (1.18)	28.28 (2.99)	0.10

Table 2. Select plasma biomarker-OCT Associations

Plasma Biomarker	OCT Metric	Noncarrier β (95% CI)	p	Carrier β (95% CI)	p	Interact on p
Aβ42/40	GCIP thickness	-349.8 (-684.1, -15.5)	0.041	-104.1 (-245.5, 37.3)	0.14	0.026
log_NfL	GCIP thickness	6.3 (-1.1, 13.6)	0.092	-2.1 (-6.2, 2.1)	0.31	0.028

Table 3. Select plasma biomarker-OCTA Associations

Plasma Biomarker	OCTA Metric	Noncarrier β (95% CI)	p	Carrier β (95% CI)	p	Interact on p
pTau217/Aβ42	6mm inner ring PD	4.43 (0.53, 8.32)	0.028	-0.05 (-1.11, 1.02)	0.93	0.020
pTau217/Aβ42	6mm inner ring VD	170.7 (15.3, 326.1)	0.033	7.36 (-35.4, 50.1)	0.73	0.029
log_NfL	6mm inner ring PD	0.05 (-0.01, 0.10)	0.096	-0.02 (-0.06, 0.01)	0.21	0.009
log_NfL	6mm inner ring VD	1.75 (-0.41, 3.91)	0.11	-0.73 (-2.17, 0.71)	0.31	0.013

- Genetic background may influence how systemic AD pathology manifests in the retina
- Clinically, warrants further investigation of integrating genotype into plasma biomarker and retinal imaging interpretation
- Personalized risk stratification + earlier detection
 - Especially in at-risk populations (ε4 carriers)
- Longitudinal data needed to validate findings



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