

Increased Foveal Avascular Zone and Subfoveal Choroidal Thickness as Potential Biomarkers of Plasma P-tau217 and Aβ42/40 in Alzheimer's

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Background

Early, non-invasive, and inexpensive biomarkers of Alzheimer's Disease (AD) suitable for mass screening that could serve as a proxy measure in prevention and intervention trials are necessary. Considering this, studies have demonstrated that ocular structures can serve as biomarkers for AD.¹ Increased foveal avascular zone (FAZ), reduced retinal nerve fibre layer (RNFL), and reduced choroidal thickness (CT) have been associated with AD progression.^{1,2} Furthermore, analysing plasma levels of AD biomarkers, including phosphorylated tau (p-tau) 217 and β-amyloid 42/40 (Aβ42/40) ratio, are increasingly being considered as a more accessible alternative to cerebrospinal fluid biomarker sampling to identify the AD stage.³ It is also known that some individuals have normal or mild cognitive impairment that remains stable, despite the presence of AD pathology in the brain, appearing resilient to AD.⁴ However, there is limited understanding of the relationship between blood-based AD biomarkers and ocular measures in older cognitively healthy individuals.

Purpose

To investigate the association between the area of the FAZ, peripapillary RNFL Thickness (pRNFLT) and subfoveal CT (sCT) with plasma p-tau217 and Aβ42/40 in cognitively healthy older individuals.

Methods

The study gained a favorable opinion from Health and Social Care Research Ethics Committee A (REC reference 22/NI/0158).

Participants:

- 45 cognitively healthy (Montreal Cognitive Assessment [MoCA] score ≥26/30) individuals (mean age: 66.1 years, range: 50-80)

Measurements:

- SD-OCT – Heidelberg Spectralis: global pRNFLT (Fig. 1) and sCT (Fig. 2)
- OCTA – Heidelberg Spectralis (Fig. 3)
- Biometry – Lenstar 900: Axial length
- Cognitive function – MoCA (Mild Cognitive Impairment screening tool) & The Kaufman Brief Intelligence Test Second Edition (KBIT-2): General cognitive abilities (composite IQ score)
- Plasma p-tau217, Aβ40 and Aβ42 concentrations (pg/mL) – Quanterix singular molecule array (Simoa) technology by the UK DRI Biomarker Factory at UCL

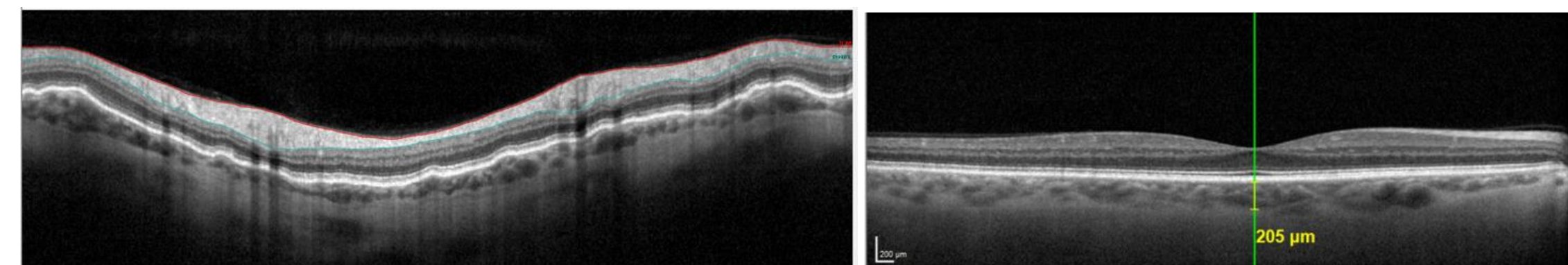


Fig. 1: Spectralis OCT measurement of global pRNFLT

Fig. 1: Spectralis OCT measurement of sCT

Results

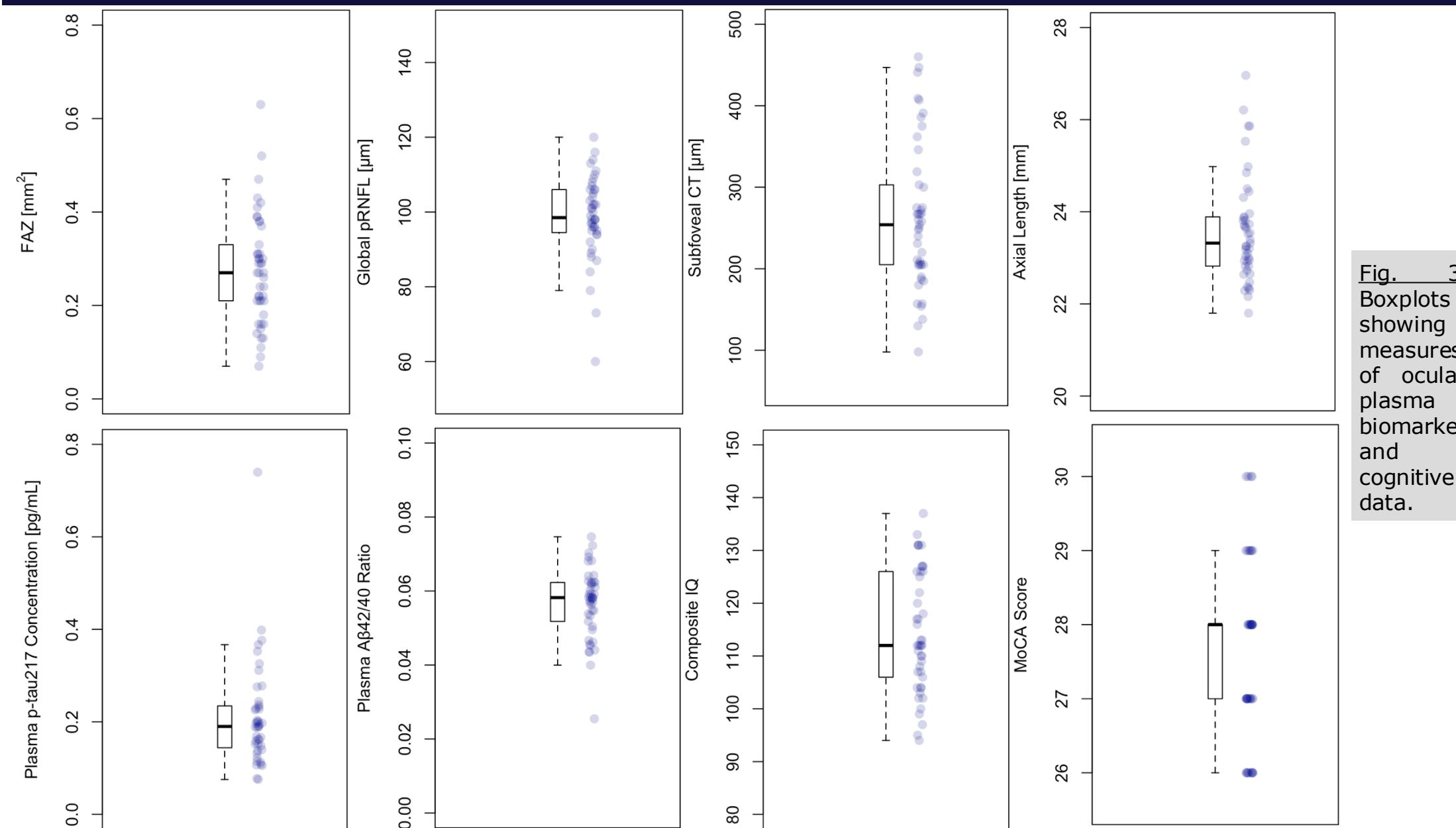


Fig. 3: Boxplots showing measures of ocular, plasma biomarker and cognitive data.

Response variables	Fixed effects	Beta coefficient	P-value
FAZ	p-tau217	0.39	0.022
	Aβ42/40 ratio	0.44	0.83
	Composite IQ	-0.0018	0.41
	MoCA	0.014	0.47
Global pRNFLT	p-tau217	9.3	0.56
	Aβ42/40 ratio	73.7	0.71
	Composite IQ	0.15	0.49
	MoCA	1.6	0.39
sCT	p-tau217	-70.0	0.57
	Aβ42/40 ratio	-4227.1	0.0068
	Composite IQ	-1.01	0.54
	MoCA	6.6	0.64

Table 1: **Multivariate linear regression models:** FAZ, global pRNFLT and sCT as outcome variables, plasma p-tau217, Aβ42/40 ratio MoCA and composite IQ scores as predictors while controlling for age, axial length and sex.

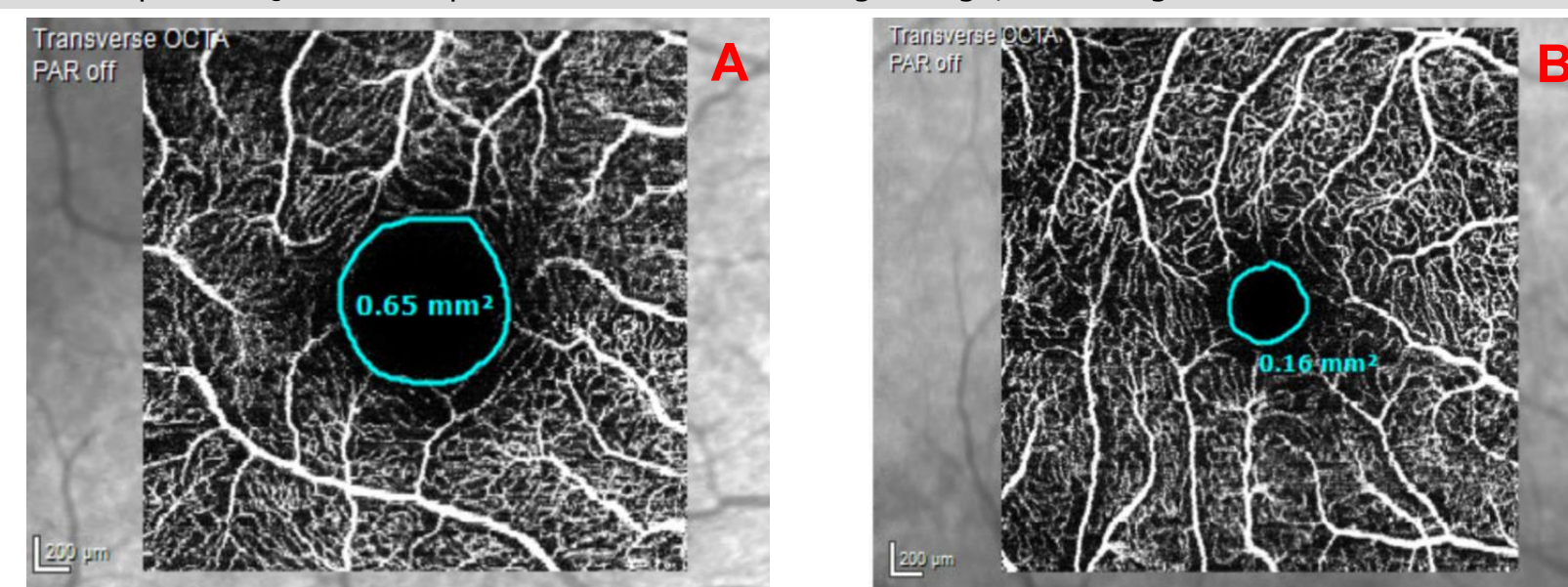


Fig. 4: OCTA scans showing (A) an enlarged FAZ (0.65 mm²) in an individual with higher plasma ptau-217 concentration (0.38 pg/mL) compared to (B) an individual with a smaller FAZ (0.16 mm²) and lower plasma ptau-217 concentration (0.20 pg/mL).

Results

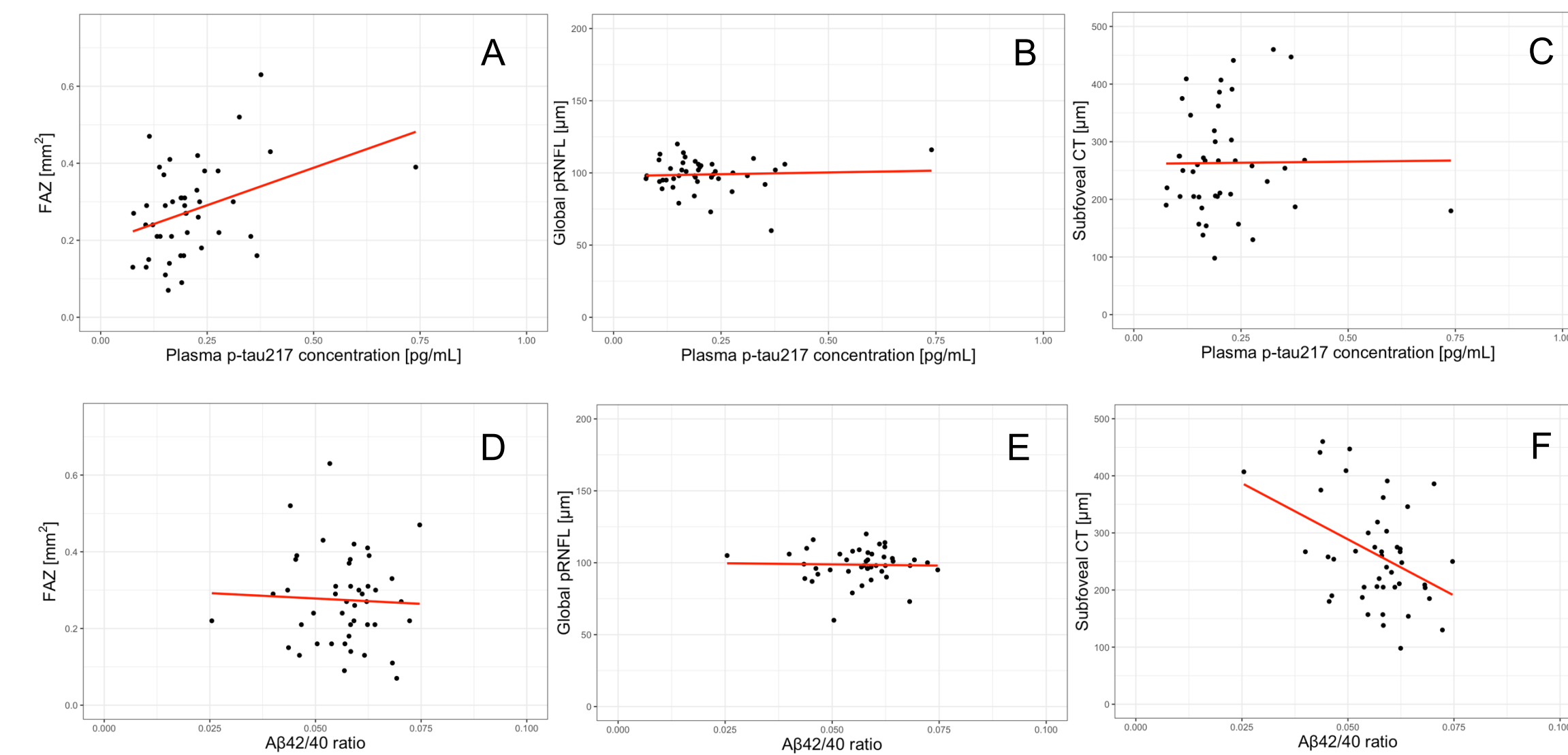


Fig. 5: FAZ (A & D), global pRNFLT (B & E) and subfoveal CT (C & F) measurements plotted against plasma p-tau217 concentration (A-C) and Aβ42/40 ratio (D-F) for cognitively healthy individuals.

Conclusions

- Cognitively healthy individuals with an enlarged FAZ exhibited higher plasma ptau-217 concentration
- An enlarged FAZ in cognitively healthy individuals may reflect decreased retinal perfusion and compensatory vascular changes in the early disease stages of AD
- Cognitively healthy individuals with increased sCT exhibited a lower Aβ42/40 ratio
- As lower Aβ42/40 ratio is associated with higher beta-amyloid plaque deposition in the brain; this could indicate a secondary inflammatory process is occurring that could be responsible for choroidal thickening
- FAZ area and sCT may be useful markers of plasma AD biomarkers

References:

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