Aqueous and plasma levels of phosphorylated tau 181 in individuals with normal cognition

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Background

- Alzheimer's disease (AD) is the most prevalent form of dementia in the Western world and there is a scientific effort aimed at identifying viable biomarkers to diagnose AD.
- The eye, specifically the retina and vitreous, have shown measurable quantities of AD biomarkers, including amyloid plaques and phosphorylated tau 181 (p-tau181).

Purpose

- To determine whether p-tau181 is detectable in the aqueous humor.
- To determine if aqueous p-tau181 is associated with other measures that might be consistent with AD such as higher plasma p-tau181 concentration and lower Montreal Cognitive Assessment (MoCA-BLIND) score.

Methods

- Aqueous humor samples, blood samples, and MoCA-BLIND scores were collected from patients who did not carry a clinical diagnosis of cognitive impairment at the time of cataract surgery.
- Aqueous p-tau181 concentrations and plasma p-tau181 concentrations were then measured using ultra-sensitive single-molecule assay ELISA technology (Quanterix SR-X).
- A rank-transformed mixed-effects multivariate regression model was used to determine associations between MoCA-BLIND scores.

Table 1: Patients Undergoing Cataract Surgery (n=16)

	Mean	Standard Deviation	Median	Range
Age (years)	71.6	6.7	71	60-83
MoCA-BLIND	20.6	1.1	20.5	19-22
Plasma p-tau181 Concentration (pg/mL)	3.2	4.0	1.99	0.66-17.7
Aqueous p-tau181 Concentration (pg/mL)	6.4	6.1	3.92	0.59-17.2
Body Mass Index (kg/m²)	25.2	5.2	24.2	18.5-40.2

Table 2: Demographic Data (n=16)

Race	n	%
Asian	1	6.25%
Black	1	6.25%
White	13	81.25%
Not Reported	1	6.25%
Sex	n	%
Female	11	68.75%
Male	5	31.25%

Results

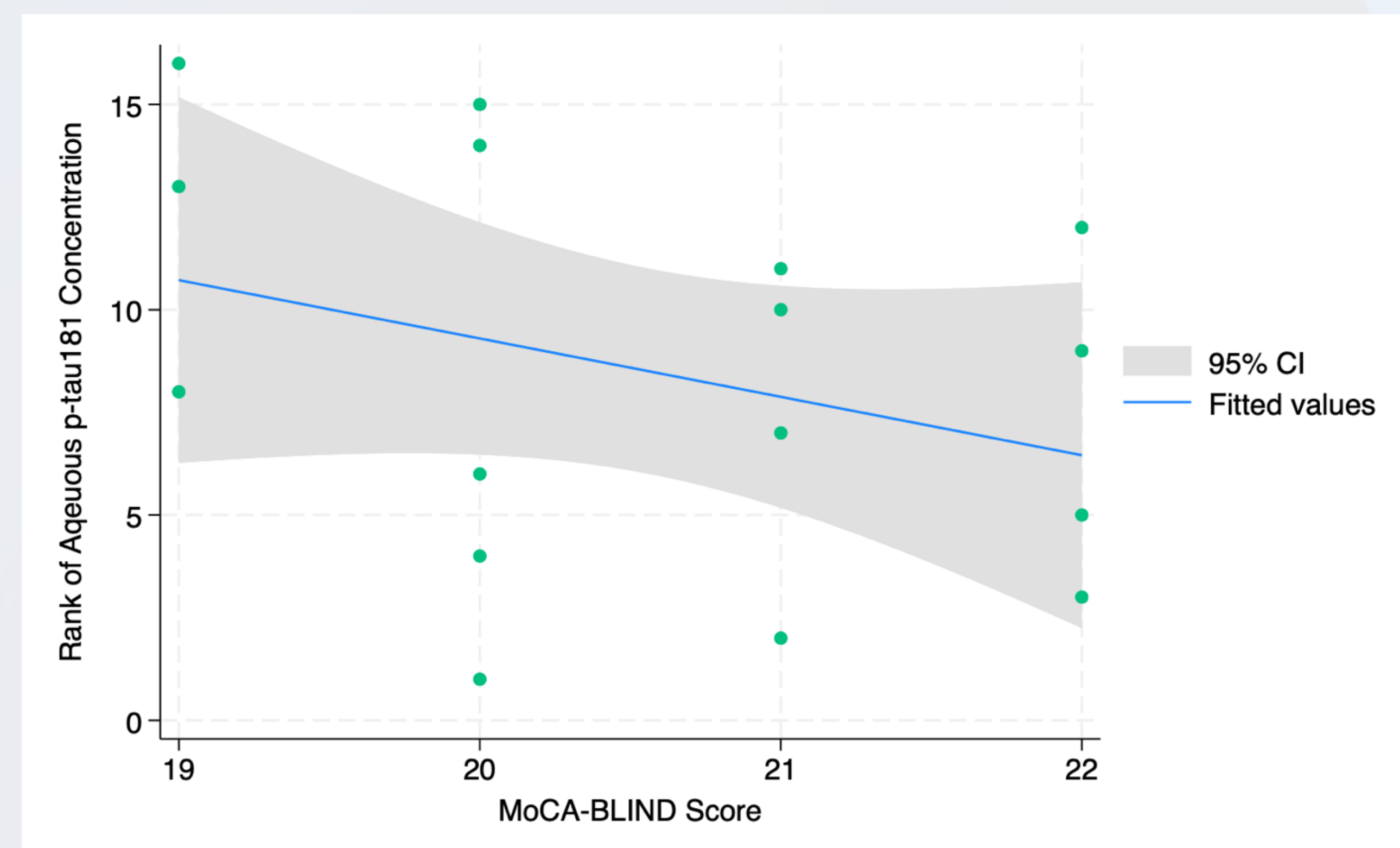Figure 1: MoCA-BLIND Score vs Rank of Aqueous p-tau181 Concentration

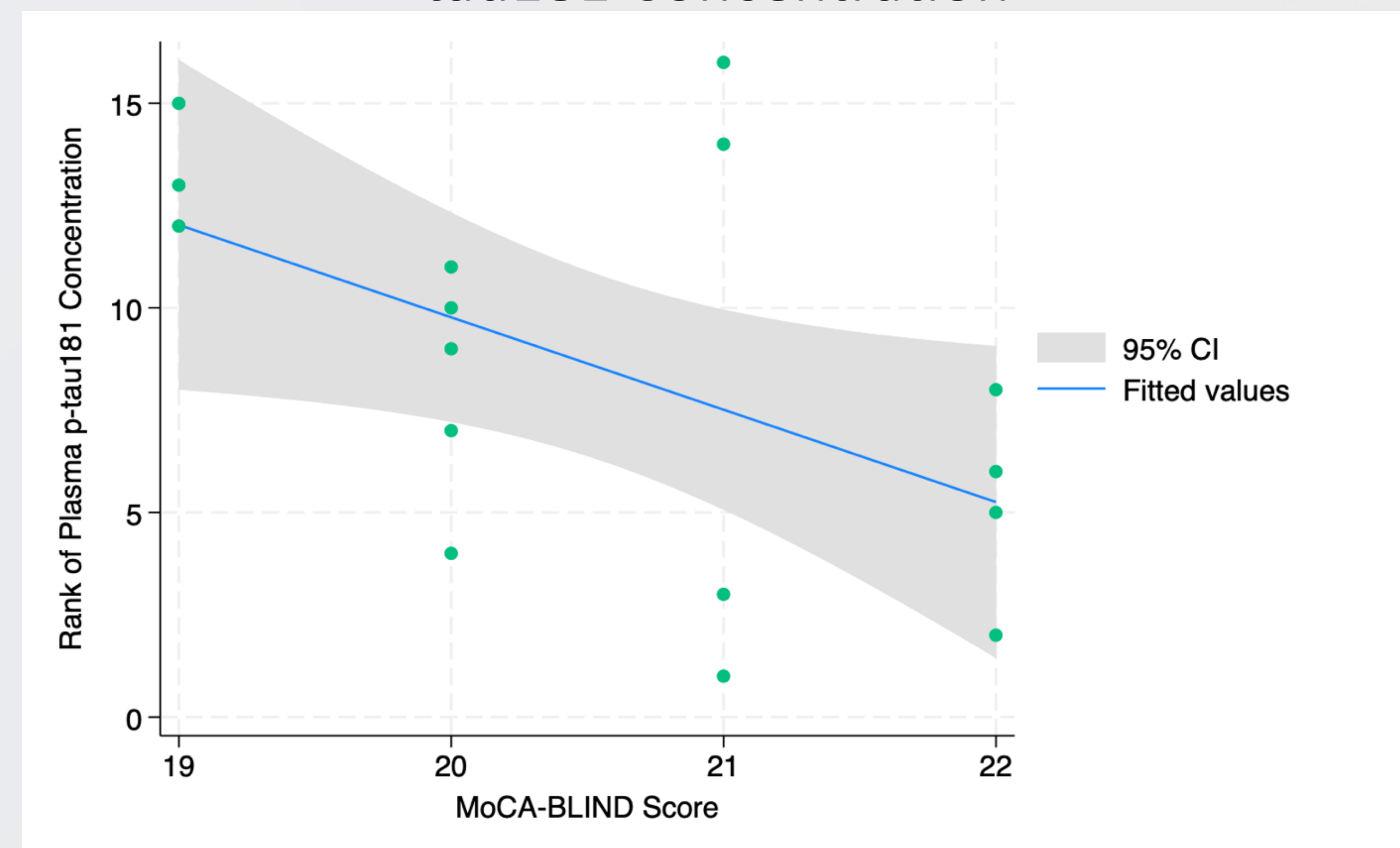Figure 2: MoCA-BLIND Score vs Rank of Plasma p-tau181 Concentration

Table 3: Regression coefficients from multivariate mixed-effects rank transformed regression model*

Explanatory Variable	Dependent Variable	Estimate	95% CI	P-value
Aqueous p-tau181**	Plasma p-tau181**	0.42	(0.76 - 0.78)	0.02
MoCA-BLIND score	Plasma p-tau181**	-0.12	(-0.19 - -0.05)	0.001
MoCA-BLIND score	Aqueous p-tau181**	-0.13	(-0.21 - -0.04)	0.005

*Multivariate regression estimates, confidence intervals, and p-values provided are controlling for age, race, sex, and BMI using a mixed-effects regression model.
**Regression results include rank transformation of the concentration of aqueous p-tau181 (pg/mL) and the concentration of plasma p-tau181 (pg/mL) to model for nonparametric relationships.

Results

Figure 3: Rank of Aqueous p-tau181 Concentration vs Rank of Plasma p-tau181 Concentration
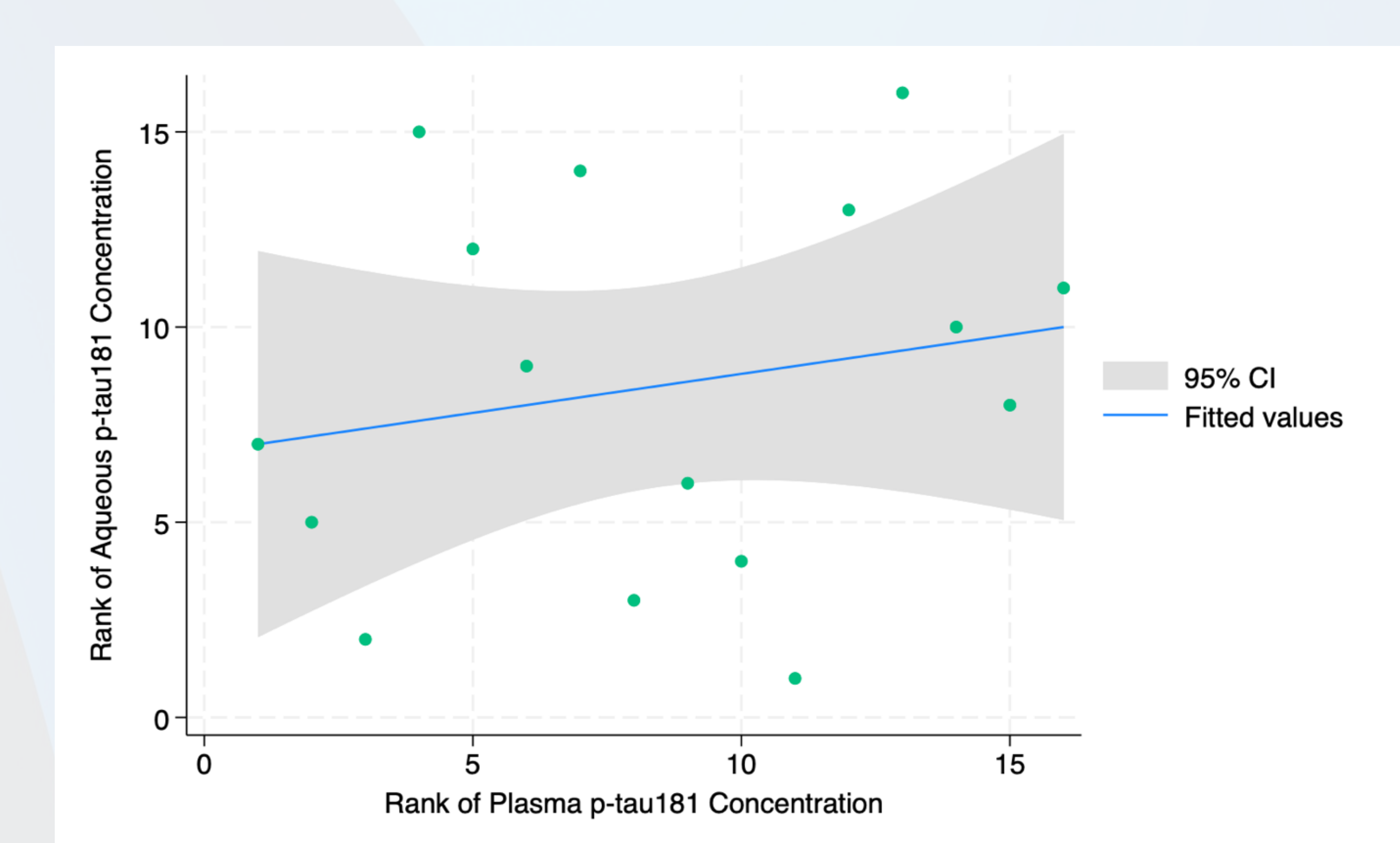
Conclusions

- **p-tau181 is measurable in aqueous humor and plasma.**
- **Its presence in the aqueous is correlated with its presence in plasma and is negatively correlated with MoCA-BLIND scores.**
- Further study in individuals with mild cognitive impairment or AD confirmed by cerebrospinal fluid and volumetric MRI metrics may yield further insight.

iMIND

Duke Ophthalmology
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References