

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

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Background: Plasma and cerebrospinal fluid (CSF) levels of p-tau181 have been associated with Alzheimer's disease (AD). The retina and vitreous have shown measurable quantities of phosphorylated tau 181 (p-tau181). The aqueous humor, which can be collected during cataract surgery, may have measurable concentrations of p-tau181.

Objective: To determine whether p-tau181 is detectable in the aqueous humor and if so, whether it 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 version 7.1) 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. A rank-transformed mixed-effects multivariate regression model was used to determine associations between aqueous concentrations, plasma concentrations, and MoCA-BLIND scores.

Results: 16 eyes of 16 participants were enrolled with an average age of 71.6. Average MoCA-BLIND score was 20.6/22, average aqueous p-tau181 concentration was 6.4 pg/mL, and average plasma p-tau181 concentration was 3.1 pg/mL. Higher plasma p-tau181 was significantly associated with higher aqueous p-tau181 ($p=0.02$). Aqueous p-tau181 and plasma p-tau181 were negatively associated with MoCA-BLIND scores ($p=0.005$ and $p=0.001$ respectively) in these patients.

Conclusion: Aqueous p-tau181 is positively correlated with plasma p-tau181 and is negatively correlated with MoCA-BLIND scores. Further study in individuals with mild cognitive impairment or AD characterized by cerebrospinal fluid and volumetric MRI metrics may yield further insights.