Scanning the eye for cognitive measures

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Introduction. Alzheimer's disease (AD) is one of the most common forms of dementia, and due to increasing life expectancy, the number of patients will continue to grow. The diagnosis of AD is supported by the use of amyloid PET scan or biomarker-based cerebrospinal fluid analyses. Currently, population-wide screening is not available since this type of testing is invasive and costly. Therefore, we propose using the eye as the window to the brain. The eye is closely connected to the brain through the optic nerve, and both develop from the neural tube. For instance, tears contain thousands of molecules and are produced by the lacrimal gland, Meibomian glands, and Goblet conjunctival cells. Protein secretion in the lacrimal gland is highly regulated by (para-)sympathetic innervation. Recent pilot data demonstrates that Aβ and Tau are detectable in tear fluid, where Tau levels were significantly elevated in AD patients compared to patients with subjective cognitive disorder. Retinal abnormalities are also observed in AD patients, which include retinal nerve fiber layer (RNFL) thinning, widespread ganglion cell loss, and optic nerve degeneration. **Aims.** We aim to investigate the association between the ocular biomarkers (in tear fluid and retinal imaging) and cognitive measures. Additionally, we aim to investigate what the predictive value of retinal imaging is for cognitive decline. **Hypothesis.** We expect that ocular biomarkers (tear tau and RNFL thickness) correlate with cognitive function and brain structure. Furthermore, we anticipate that cognitive decline can be predicted by retinal vascular parameters and RNFL thickness. **Methods.** Data from the Maastricht Study will be used, which is an ongoing observational prospective population-based cohort study that includes 9000 participants. Tear fluid will be collected with the use of Schirmer strips, and fundus imaging will be used to obtain images of the posterior chamber of the eye. Additionally, cross-sectional images of the retina will be obtained through OCT imaging. The level of tear biomarkers related to AD will be determined by biochemical analyses. **Relevance.** Early diagnosis of AD is important to promote timely and optimal management. On top of that, future therapies may be more effective when started earlier in the disease.

Keywords. Ocular biomarkers, Tear fluid, Alzheimer's Disease.