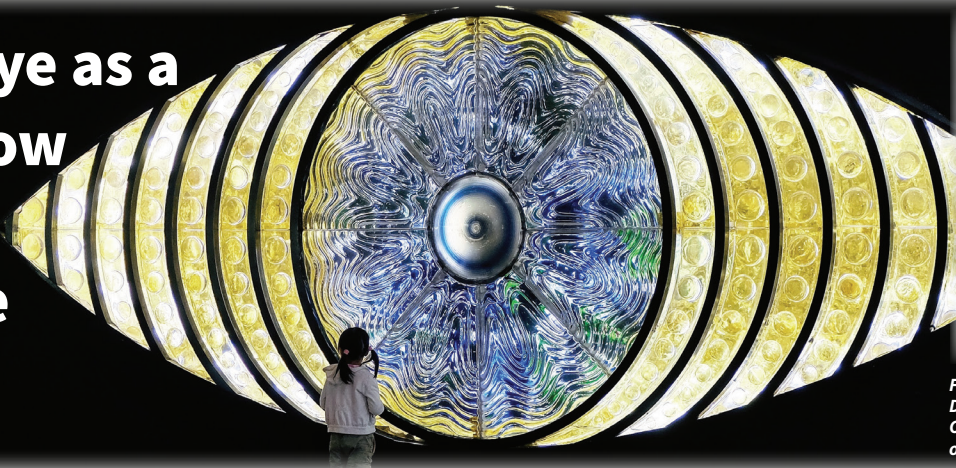


The eye as a window to the brain



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On June 22, 2023, Frederik Pedersen defended his thesis, “Diabetic retinopathy as a marker of cognitive dysfunction and depression: A clinical and epidemiological approach,” at the Dept. of Ophthalmology, Odense University Hospital, University of Southern Denmark. The main supervisor was Professor Jakob Grauslund, M.D., Ph.D., D.M.Sc., Dept. of Ophthalmology, Odense University Hospital, Dept. of Clinical Research, University of Southern Denmark, Steno Diabetes Centre Odense, Denmark. The co-supervisors were Associate Professor Lonny Stokholm, scient.san.publ, Ph.D., Dept. of Clinical Research, University of Southern Denmark; Professor Tunde Peto, M.D., Ph.D., Centre for Public Health, Queen’s University Belfast, Northern Ireland, UK; and Professor Frans Pouwer, Ph.D., Dept. of Medical Psychology, Amsterdam UMC, The Netherlands.

In recent years, retinal neurodegeneration has been recognized as an early event in diabetic retinopathy (DR). Given that the eye and brain share similar embryologic origins, anatomical features, and physiological properties, observations suggest that the retina provides a unique “window” to the brain. Systemic neurodegenerative diseases, such as Alzheimer’s disease and depression, have been linked to diabetes, but less is known regarding their association with DR. With a register-based and clinical approach, this dissertation thus aimed to investigate DR as a marker of Alzheimer’s disease and

depression, using real-world data. It also aimed to explore in a clinical setting whether non-invasive retinal parameters were associated with mild cognitive impairment, a pre-state of dementia, in individuals with type 2 diabetes.

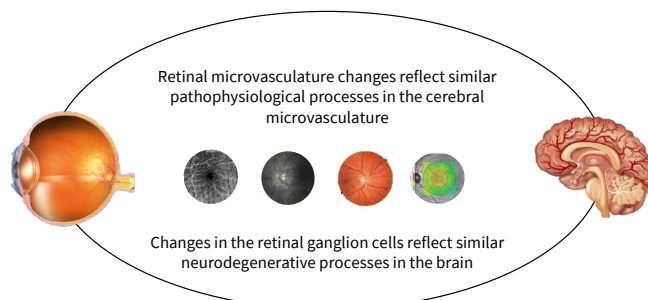
We first evaluated the risk of Alzheimer’s disease in patients with DR. Patients with DR had a 34% increased risk of Alzheimer’s disease compared to patients with diabetes without DR. We then examined the bidirectional association between depression and DR in patients with type 2 diabetes. In this epidemiological study of more than 240,000

Key points:

- DR was associated with a significantly increased risk of Alzheimer’s disease.
- We found no indication of a bidirectional association between DR and depression in patients with type 2 diabetes.
- Old age with type 2 diabetes and mild cognitive impairment was associated with retinal structural alterations compared to cognitively healthy controls.

patients with type 2 diabetes, we did not find DR to be independently associated with depression. Finally, we examined the association between retinal non-invasive parameters and mild cognitive impairment. In this observational cross-sectional study, we included elderly patients with type 2 diabetes without known retinal diseases except for non-proliferative DR. All participants had a broad neuropsychological evaluation performed to determine their cognitive status. Based on this evaluation, participants were divided into two groups: those with mild cognitive impairment and those without cognitive impairment. We then performed retinal examinations including retinal oximetry, color fundus photography, optical coherence tomography (OCT), and OCT-angiography. Patients with mild cognitive impairment had a thinner macular ganglion cell layer and macular retinal nerve fiber layer compared to patients without cognitive impairment. In contrast, we found no differences in retinal microvascular or oximetry parameters between the groups.

Figure 1. The retina may be a window to study neurodegenerative disorders due to the common anatomical and physiological properties. This might involve non-invasive retinal parameters. For the clinical study, we utilized (from left to right) optical coherence tomography (OCT) angiography, retinal oximetry measurements, color fundus photos and OCT to assess various retinal parameters and their association to mild cognitive impairment



References

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Future directions:

- Future studies should use longitudinal designs to investigate how retinal parameters can be used to detect and monitor cognitive impairment.