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The retina: a new observation window of the neuropathic process in type 1 diabetes

Aims: To assess whether the retinal nerve fiber layer (RNFL) thickness can be used as an indicator for systemic neurodegeneration in patients with type 1 diabetes (T1DM).
Methods: Thirty-eight adults with T1DM and established diabetic neuropathy (DN) were studied (data from EUDRA CT: 2013-004375-12). Optical coherence tomography was obtained in order to study RNFL thickness and central foveal thickness. Nerve conduction velocities were recorded using standardized neurophysiologic testing of the tibial and peroneal motor nerves and the radial and median sensory nerves. 24-hour electrocardiographic recordings were used to achieve time- and frequency-domain measures of heart rate variability (HRV), and a pain catastrophizing scale was used to evaluate cognitive distortion.
Results: When adjusted for hemoglobin A1c, RNFL thickness was positively associated with nerve conduction velocities of the sensory and motor nerves (all $p<0.036$) and negatively associated with time- and frequency-domain measures of HRV (all $p<0.033$). Moreover, RNFL thickness was negatively associated with catastrophic thinking (all $p<0.038$).
Conclusions: RNFL thickness was associated with measures of peripheral and autonomic DN and could become an indicator of systemic neurodegeneration.

Comments. In literature, there is already evidence that retinal neurodegeneration could be present before or in absence of diabetic retinopathy (Neriyanuri S et al *Br J Ophthalmol. 2017;101:1174-1178*) and that different retinal layers could be affected in patients with DN, in comparison to those without DN (Liu B et al *Curr Eye Res. 2021;46:1201-1208;`Choi JA et al PLoS One.2017;12:1–14*). In this cross-sectional study, an association between the RNFL thickening and the worsening of peripheral and autonomic measures of DN in patients with long-term T1DM was described, speculating the dominant presence of edema of RNFL (beyond the cellular apoptosis) as part of neurodegenerative processes. Despite some limitations (the small sample size, the lack of a healthy control group and the absence of cardiovascular reflex tests), these data described that the retina, as a part of the nervous system, could be involved in the neuropathic process, as observed in other neurodegenerative diseases (Vujosevic S et al *Eye (Lond). 2023;37:379*). However, the evolution of the retinal neurodegeneration (and its association with DN) has not yet been well defined with some conflicting findings. Of course, the observation of all the retinal layers could help us to understand if the swelling of the RNFL could be matched with the thinning of other parts of the structure. Moreover, the longitudinal observation of these changes in children and adolescents with T1DM could clarify whether the RNFL thickness could predict the incidence and severity of systemic neurodegeneration.
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Reference. Brock C, Wegeberg AM, Nielsen TA, Karout B, Hellström PM, Drewes AM, Vorum H. The retinal nerve fiber layer thickness is associated with systemic neurodegeneration in long-term type 1 diabetes. Transl Vis Sci Technol. 2023;12(6):23. doi: 10.1167/tvst.12.6.23. PMID: 37367720; PMCID: PMC10309163.
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