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Association of Retinal Changes With Alzheimer Disease Neuroimaging Biomarkers in Cognitively Normal Individuals.

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IMPORTANCE: Retinal biomarkers reflecting in vivo brain Alzheimer disease (AD) pathologic abnormalities could be a useful tool for screening cognitively normal (CN) individuals at the preclinical stage of AD. OBJECTIVES: To investigate the association of both functional and structural alterations of the retina with in vivo AD pathologic abnormalities in CN older adults and model a screening tool for detection of preclinical AD. DESIGN, SETTING, AND PARTICIPANTS: This cross-sectional study included a total of 49 CN individuals, and all assessment was done at the Seoul National University Hospital, Seoul, South Korea. All participants underwent complete ophthalmic examination, including swept-source optical coherence tomography (SS-OCT) and multifocal electroretinogram as well as amyloid-β (Aβ) positron emission tomography and magnetic resonance imaging. Data were collected from January 1, 2016, through October 31, 2017, and analyzed from February 1, 2018, through June 30, 2020. MAIN OUTCOMES AND MEASURES: For structural parameters of the retina, the thickness of the macula and layer-specific thicknesses, including peripapillary retinal nerve fiber layer and ganglion cell-inner plexiform layer measured by SS-OCT, were used for analysis. For functional parameters of the retina, implicit time and amplitude of rings 1 to 6 measured by multifocal electroretinogram were used. RESULTS: Of the 49 participants, 25 were women (51.0%); mean (SD) age was 70.6 (9.4) years. Compared with 33 CN individuals without Aβ deposition (Aβ-CN), the 16 participants with Aβ (Aβ+CN) showed reduced inner nasal macular thickness (mean [SD], 308.9 [18.4] vs 286.1 [22.5] μm; P = .007) and retinal nerve fiber layer thickness, particularly in the inferior quadrant (133.8 [17.9] vs 103.8 [43.5] μm; P = .003). In addition, the Aβ+CN group showed prolonged implicit time compared with the Aβ-CN group, particularly in ring 5 (41.3 [4.0] vs 38.2 [1.3] milliseconds; P = .002). AD-related neurodegeneration was correlated with the thickness of the ganglion cell-inner plexiform layer only (r = 0.41, P = .005). The model to differentiate the Aβ+CN vs Aβ-CN groups derived from the results showed 90% accuracy. CONCLUSIONS AND RELEVANCE: The findings of this study showing both functional as well as structural changes of retina measured by multifocal electroretinogram and SS-OCT in preclinical AD suggest the potential use of retinal biomarkers as a tool for early detection of in vivo AD pathologic abnormalities in CN older adults.

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