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THE AGE-RELATED CHANGES IN VERTEBRATE RETINA: INSIGHTS FROM STUDIES IN INBRED AND OUTBRED MOUSE STRAINS

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The vertebrate retina is a complex and highly organized tissue that plays a critical role in vision. As individuals age, the retina undergoes a variety of changes, including a decline in photoreceptor function, thinning of the layers, and alterations in the structure and function of glial retinal cells, that can impact visual function [1]. Such changes have been associated with a variety of visual disorders, including age-related macular degeneration and diabetic retinopathy [2,3]. Understanding the molecular mechanisms underlying these alterations is crucial for developing effective therapies to treat these disorders. Animal models provide valuable tools to study the aging of the retina and, based on their different genetic background, the combinatory use of both inbred and outbred mouse strains may lead to a more comprehensive understanding of the aging process. In this context, we propose a multimodal approach to identify and characterize stages of age-related retinal degeneration with high temporal resolution. To this end, we conducted in vivo, and ex vivo analyses using optical computed tomography (OCT), electroretinogram (ERG) and immunofluorescence (IF) experiments, respectively, to estimate the age-dependent decline of retina function. Mouse retinas from two different strains, an inbred (C57BL/6) and an outbred (CD-1), both male and female, were analyzed at four different time points (2, 6, 12, and 18 months). The research was approved by the Ministry of Health with protocol 1177/2020-PR. OCT provided structural information on the thickness of each retinal layer, documenting a decrease in retinal thickness associated with aging. ERG measures the light-induced electrical activity of the retina, and results indicate a progressive reduction of amplitudes of both a- and b- waves. Additionally, we conducted IF using retinal-specific markers to label key retinal structures, such as GNAT-2 for photoreceptor cells (PRCs), PKCα for rod bipolar cells (RBCs) and Calbindin for horizontal cells (HCs). We also investigated synaptophysin as a marker of cell synapses between photoreceptors and horizontal cells. Consistent with the in vivo data, IF analysis demonstrated a significant age-dependent reduction of PRCs, HCs, RBCs, as well as the area of synapses between PRCs and HCs. Taken together these findings demonstrate a decline in retinal layers associated with aging and suggest potential implications for age-related visual impairment in both mouse strains.

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