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Review: Tauopathy in the retina and optic nerve: does it shadow pathological changes in the brain?

Wing-Lau Ho,[1] Yen Leung,[1] Andrea Wing-Ting Tsang,[1] Kwok-Fai So,[2,3] Kin Chiu,[1] Raymond Chuen-Chung Chang[1,2,3]

[1]Laboratory of Neurodegenerative Diseases, Department of Anatomy, LKS Faculty of Medicine; The University of Hong Kong, Pokfulam, Hong Kong SAR, China; [2]Research Centre of Heart, Brain, Hormone and Healthy Aging, LKS Faculty of Medicine; The University of Hong Kong, Pokfulam, Hong Kong SAR, China; [3]State Key Laboratory of Brain and Cognitive Sciences, The University of Hong Kong, Pokfulam, Hong Kong SAR, China

Tau protein's versatility lies in its functions within the central nervous system, including protein scaffolding and intracellular signaling. Tauopathy has been one of the most extensively studied neuropathologies among the neurodegenerative diseases. Because the retina and optic nerve are parts of the central nervous system, we hypothesize that tauopathy also plays a role in various eye diseases. However, little is known about tauopathy in the retina and optic nerve. Here, we summarize the findings from histopathological studies on animal models and human specimens with distinct neurodegenerative diseases. Similar pathological changes of tau protein can be found in Alzheimer's disease, frontotemporal lobe dementia, and glaucoma. In view of the important roles of tauopathy in the brain, it is hoped that this review can stimulate research on eye diseases of the retina and optic nerve.

NEURODEGENERATION AND THE RETINA: Neurodegeneration is a collective term for the progressive loss of the structure, function, or even death of neurons. The pathogenesis of neurodegeneration involves the aberrant processing, misfolding, and subsequent aggregation of normal proteins that are then deposited both intracellularly and extracellularly. At the molecular level, it involves mechanisms such as defective neuronal plasticity through aberrant regenerative responses, reduced levels of neurotrophins, and increased neuronal vulnerability to stress. At least three types of abnormally aggregated proteins have been found. These include β-amyloid (Aβ) peptides in the neuritic plaques of Alzheimer's disease (AD), the fibrillation of tau protein to form neurofibrillary tangles in AD and Pick bodies in frontotemporal dementia (FTD), and alpha-synuclein in the Lewy bodies of Parkinson disease (PD) and in Lewy body disease [1,2].

The retina is part of the central nervous system (CNS), with various cell types comprising of photoreceptors, bipolar cells, horizontal cells, amacrine cells, and retinal ganglion cells (RGCs). The axons of RGCs forming the last stop of the relay merge to form the optic nerve, optic chiasm, and optic tract, which ultimately forms synapses at the lateral geniculate nucleus of the thalamus. Therefore, the retina and optic nerve could be affected by similar degenerative processes during neurodegeneration.

Evidence suggests that the visual system is affected by neurodegenerative processes in AD. Cognitive visual changes have been reported in patients in the early stages of AD, including difficulties in reading and finding objects [3-5], depth perception, perceiving structure from motion [3,5-7], color recognition [3,8], and impairment of spatial contrast sensitivity [6,9]. Previously, all these defects were considered to be due to pathological changes in the cortex. With the development of modern ocular imaging techniques, recent findings demonstrate that pathological changes within the retina could be found in these patients. Optic coherent tomography has demonstrated a significant reduction of peripapillary retinal fiber layer (RFL) thickness in patients with early AD when compared with age-matched controls [10-14]. The thinning of the RFL was observed predominantly in the inferior and superior quadrants, which was consistent with the inferior and superior visual field loss in AD [3,11]. Reduction of the macular thickness has also been reported in AD, and the total volume of the macula was inversely correlated with the severity of the disease [12]. Changes in the optic nerve head have been observed, using confocal scanning laser ophthalmoscopy. The observed changes included reduced RFL thickness, neuroretinal rim volume and area, and an increased cup–disc ratio, suggesting an overall reduction in the number of optic nerve fibers passing through the optic nerve head [15]. Moreover, laser Doppler flowmetry has

Correspondence to: Raymond Chuen-Chung Chang, Rm. L1-49, Laboratory Block, Faculty of Medicine Building, 21 Sassoon Road, Pokfulam, Hong Kong SAR, China Phone: +852 28199127; FAX: +852 28170857; email: rccchang@hku.hk