Increased oxidative stress and apoptotic cell death is closely correlated with reactive astrogliosis, altering their structural and functional properties in the aging retina

Mansour, H.[1], Braidy, N.[2], Arfuso, F.[3], Sarafian, R.Y.[1], Cole, L.[4], Weible II, M.[5], Poljak, A.[2], Grant, R.[6], Sachdev, P.S.[2] and Chan-Ling, T.[1]

[1] Discipline of Anatomy and Histology, School of Medical Sciences and Bosch Institute, Sydney Medical School, University of Sydney, Camperdown, NSW 2006, Australia, [2] Centre for Healthy Brain Ageing, School of Psychiatry, UNSW Medicine, Randwick, NSW 2031, Australia, [3] School of Biomedical Sciences, Faculty of Health Sciences, Curtin University, Bentley, Perth, WA 6102, Australia, [4] Microbial Imaging Facility, ithree institute, University of Technology Sydney, Ultimo, NSW 2007, Australia, [5] Eskitis Institute, School of Natural Sciences, Griffith University, Nathan, QLD 4111, Australia, [6] Australasian Research Institute, Sydney Adventist Hospital, Wahroonga, NSW 2076, Australia

Aging affects many structural and functional properties that are regulated by astrocytes, such as synaptic plasticity, gap junction communication, and water/ion metabolic balance. Cumulative oxidative stress alters glial phenotypic and gene expression, initiating aberrant changes in cell viability, leading to dysfunction and impaired responses. In this study, we examined the retina as an ideal model of the central nervous system (CNS). We employed a multimodal approach using a combination of advanced technologies and high-end applications including multiplex immunohistochemistry, confocal laser scanning microscopy, online emission fingerprinting, and Bitplane Imaris 3D-visualisation and image processing, to provide well-defined qualitative and quantitative data analysis. Retinal whole-mounts were prepared from Wistar rats of four distinct age groups that included developing (postnatal day 0, 2, 5, and 12), young adult (3 months old), middle aged (9 months old), and aged (18, 22, and 31 months old).

Our main findings show that aging leads to overall increases in oxidative stress (i.e. decreased nicotinamide adenine dinucleotide (NAD+/NADH) ratio content, increased protein carbonyl formation and poly ADP ribose polymerase (PARP) enzymatic activity), as well an increase in apoptotic cell death among astrocytes and retinal ganglion cells. In our Western blot and immunoreactivity data, we showed an age-related decline in drebrin, ezrin, connexin43 (Cx43), nestin, vimentin, pax2, and betaIII-tubulin, except for glial fibrillary acidic protein (GFAP), in the retina. We demonstrated further that astrocytic metabolic markers glutamine synthetase (GS), kynurenine-aminotransferase II (KATII), and aquaporin4 (AQP4) are highly expressed in the middle-aged groups. In short, our study shows that the NAD+/NADH ratio is necessary for maintenance of normal cellular function, and a direct link exists between oxidative stress, cell death, and retinal aging.

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