Glaucoma pathogenesis and neurotrophins: Focus on the Molecular and Genetic basis for Therapeutic prospects

Chitranshi N (1), Dheer Y (1), Abbasi M (1), You Y (2), Graham SL (1), Gupta V (1)

1 Faculty of Medicine and Health Sciences, Macquarie University, F10A, 2 Technology Place, North Ryde, NSW 2109, Australia.
2 Save Sight Institute, Sydney University, Sydney NSW 2000, Australia.

BACKGROUND: Retinal ganglion cell (RGC) degeneration is a major feature of glaucoma pathology. Neuroprotective approaches that delay or halt the progression of RGC loss are needed to prevent vision loss which can occur even after conventional medical or surgical treatments to lower intraocular pressure.

OBJECTIVE: The aim of this review was to examine the progress in genetics and cellular mechanisms associated with endoplasmic reticulum (ER) stress, RGC dysfunction and cell death pathways in glaucoma.

MATERIAL AND METHODS: Here, we review the involvement of neurotrophins like brain derived neurotrophic factor (BDNF) and its high affinity receptor tropomyosin receptor kinase (TrkB) in glaucoma. The role of ER stress markers in human and animal retinas in health and disease conditions is also discussed. Further, we analysed the literature highlighting genetic linkage in the context of primary open angle glaucoma and suggested mechanistic insights into potential therapeutic options relevant to glaucoma management.

RESULTS: The literature review of the neurobiology underlying neurotrophin pathways, ER stress and gene associations provide critical insights into association of RGCs death in glaucoma. Alteration in signalling pathway is associated with increased risk of misfolded protein aggregation in ER promoting RGC apoptosis. Several genes that are linked with neurotrophin signalling pathways have been reported to be associated with glaucoma pathology.

CONCLUSION: Understanding genetic heterogeneity and involvement of neurotrophin biology in glaucoma could help to understand the complex pathophysiology of glaucoma. Identification of novel molecular targets will be critical for drug development and provide neuroprotection to the RGCs and optic nerve.

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