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Neurotrophic protection of retinal ganglion cells in a mouse model of ocular hypertension

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Abstract

Our long-term goal is to determine how neurotrophins can be used to protect retinal ganglion cells (RGCs) in glaucoma. Glaucoma is a group of neurodegenerative diseases characterized by RGC death. Unfortunately, how an RGC degenerates before death is poorly understood. Brain-derived neurotrophic factor (BDNF), one of the neurotrophins essential for neuronal survival and function in the central nervous system, acts as a neuroprotective agent to maintain RGC health, but little is known about whether and how BDNF protects retinal circuitry and visual function against the insults of glaucoma. Combining mouse genetics, imaging, physiological techniques and behavioral assays, we investigated the structural and functional degeneration of RGCs, and the underlying neuroprotective mechanisms of BDNF in glaucoma. We have established a mouse model of laser-induced chronic ocular hypertension to mimic human high-tension glaucoma. We find that dendritic atrophy of RGCs is subtype- and location-dependent in hypertensive eyes. With a large-scale multi-electrode array, we examined the degeneration of visual response properties of RGCs in hypertensive eyes. We also quantified the vision loss using an optomotor response test. Using an inducible Cre-mediated recombination system, we will overexpress BDNF in RGCs when ocular hypertension is induced. We will determine whether BDNF prevents RGC degeneration in a subtype-specific manner. In summary, our study provides a comprehensive assessment of the nature of glaucomatous damage on RGCs and should add new insight to the neuroprotective mechanisms of BDNF and herald new therapies for glaucoma patients.

Biography

Xiaorong Liu has completed her Ph.D. in 2002 from University of Virginia and postdoctoral studies from University of California San Francisco in 2007. She is an assistant professor of Ophthalmology and Neurobiology at Northwestern University, studying the retinal ganglion cell development and degeneration in mice.