

# Anesthetic Preconditioning as Endogenous Neuroprotection in Glaucoma

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Blindness in glaucoma is the result of death of Retinal Ganglion Cells (RGCs) and their axons. RGC death is generally preceded by a stage of reversible dysfunction and structural remodeling. Current treatments aimed at reducing intraocular pressure (IOP) are ineffective or incompletely effective in management of the disease. IOP-independent neuroprotection or neuroprotection as adjuvant to IOP lowering in glaucoma remains a challenge as effective agents without side effects have not been identified yet. We show in DBA/2J mice with spontaneous IOP elevation and glaucoma that the lifespan of functional RGCs can be extended by preconditioning RGCs with retrobulbar lidocaine in one eye at four months of age that temporarily blocks RGC axonal transport. The contralateral, PBS-injected eye served as control. Lidocaine-induced impairment of axonal transport to superior colliculi was assessed by intravitreal injection of cholera toxin B.

Long-term (nine months) effect of lidocaine were assessed on RGC electrical responsiveness (PERG) , IOP, expression of relevant protein (BDNF, TrkB, PSD95, GFAP, Synaptophysin, and GAPDH) and RGC density. While lidocaine treatment did not alter the age-related increase of IOP, TrkB expression was elevated, GFAP expression was decreased, RGC survival was improved by 35%, and PERG function was preserved. Results suggest that the lifespan of functional RGCs in mouse glaucoma can be extended by preconditioning RGCs in early stages of the disease using a minimally invasive treatment with retrobulbar lidocaine, a common ophthalmologic procedure. Lidocaine is inexpensive, safe and is approved by Food and Drug Administration (FDA) to be administered intravenously.

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