

# Ocular hypertension impairs optic nerve axonal transport leading to progressive retinal ganglion cell degeneration

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Ocular hypertension (OHT) is the main risk factor of glaucoma, a neuropathy leading to blindness. Here we have investigated the effects of laser photocoagulation (LP) -induced OHT, on the survival and retrograde axonal transport (RAT) of adult rat retinal ganglion cells (RGC) from 1 to 12 wks. Active RAT was examined with fluorogold (FG) applied to both superior colliculi (SCi) 1 wk before processing and passive axonal diffusion with dextran tetramethylrhodamine (DTMR) applied to the optic nerve (ON) 2 d prior to sacrifice.

Surviving RGCs were identified with FG applied 1 wk pre-LP or by Brn3a immunodetection. The ON and retinal nerve fiber layer were examined by RT97-neurofibrillar staining. RGCs were counted automatically and color-coded density maps were generated. OHT retinas showed absence of FG+ or DTMR+RGCs in focal, pie-shaped and diffuse regions of the retina which, by two weeks, amounted to, approximately, an 80% of RGC loss without further increase. At this time, there was a discrepancy between the total number of surviving FG-prelabelled RGCs and of DMTR+RGCs, suggesting that a large proportion of RGCs had their RAT impaired.

This was further confirmed identifying surviving RGCs by their Brn3a expression. From 3 weeks onwards, there was a close correspondence of DTMR+RGCs and FG+RGCs in the same retinal regions, suggesting axonal constriction at the ON head. Neurofibrillar staining revealed, in ONs, focal degeneration of axonal bundles and, in the retinal areas lacking backlabeled RGCs, aberrant staining of RT97 characteristic of axotomy.

LP-induced OHT results in a crush-like injury to ON axons leading to the anterograde and protracted retrograde degeneration of the intraocular axons and RGCs.

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