NEW DIRECTIONS IN GLAUCOMA RESEARCH
NUEVOS CAMINOS EN LA INVESTIGACIÓN DEL GLAUCOMA

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Retinal ganglion cells in experimentally induced glaucoma do not die at the same time, but rather the process is protracted over the course of several months. Therefore, the progression of this optic neuropathy over the time provides avenues in which to study the state of still-living cells and to save them from death. The signal for apoptotic cell death is either not received by all RGCs at the same time or that they respond differentially in glaucomatous eyes. RGCs death is the direct insult of a primary pathological process in glaucoma and additionally may be the result of dying RGCs effect on the surrounding uninjured RGCs. Specific initiators of apoptosis in glaucoma may include blockage of axonal transport and neurotrophin depletion; glutamate excitotoxicity; antibodies to heat shock proteins; ischemia; and nitric oxide synthase upregulation with reactive oxygen species formation. In the primate retina, following loss of RGCs there is continuous atrophy of the surviving cells that leads to visual dysfunction. The transneuronal changes in the glaucomatous primates leads to the loss of some and a reduction of other cell soma sizes of the lateral geniculate nucleus, the target of optic axons. Functional assessment of visual changes in glaucoma patients using fMRI method showed a loss of visual function that correlated nicely with the loss of visual field in the eye (Duncan et al.) (1). Can this method assess changes in the early stages of glaucoma before RGCs death? The fMRI studies in macular degeneration patients with losses of foveal vision showed extensive activity in the cortical foveal area (Baker et al.) (2) and points to the extensive reorganization of visual terminal areas. It is reasonable to assume that in macular degeneration some foveal retinal cells survived and these RGCs cells expanded their projections in the cortex or parafoveal RGC axons invaded the territory in the foveal area of the cortex. In the rat glaucoma (King et al.) (3), the visual scotoma was not apparent in the tectum (terminal areas of optic axons) in the early period and larger receptive fields on the periphery represent the early signs of altered geometry of the retina. We assumed that following the death of larger cells on the periphery, the remaining ganglion cells expanded their axonal arbors in the tectum leading to the enlarged receptive fields. The relationship of duration and magnitude of IOP elevation showed a significant positive correlation between percentages of receptive field sizes in the tectum of glaucomatous rat. This correlation become evident after six months of sustained elevated IOP. A greater increase in visual receptive field size correlates well with a greater increase in the IOP. An increase in the visual receptive field may represent a very long term effect of the remaining ganglion cells in the glaucomatous eyes in which ganglion cell axons try to compensate for the loss of the fields by occupying a larger than normal terminal territory (King et al.) (3). In primates glaucoma RGC death leads to changes in the lateral geniculate nucleus and VI where cell loss and the shrinkage of LGN was reported (Yucel et al.) (4). Cytochrome oxidase activity decreased in the ocular dominant columns subserving the glaucomatous eye. These changes in glaucomatous animal led the authors to describe glaucoma as a neurodegenerative disease. To date it is evident that the initiation of the elevated IOP trigger changes in the retina as well as in the CNS target centers whose effect continuous for a very long time.

The continuous debate on the «dogma» of glaucoma, i.e. whether ganglion cells die first or optic

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Prof. Sharma has introduced revolutionary advances in the experimental glaucoma field. He established the first model of glaucoma in rat that until today is the most used method of cauterizing the episcleral veins. He for the first time described that RGCs die by apoptosis in glaucoma, and has published many papers on the mechanisms of cell death and survival of retinal ganglion cells during glaucoma.
axons are damaged first, has yet to be resolved. In both situations changes commence in the termination nuclei of the visual pathways. The dramatic change seen in the visual centers in glaucomatous animal beg the question that the functional relationship between the loss or degradation of the visual fields and the changes in visual acuity and visual thresholds must be explored. The ability of the neuronal system to undergo remodeling and repair following injury is influenced by interactions between the remaining viable RGCs in glaucomatous retina as well as by the response of individual cells to the reduction in IOP and the administration of neuroprotective agents. If by reducing the IOP and/or administration of neuroprotective agents one can determine the functional consequences of retina leading either to partial or complete restitution of function, it may offer a new avenue for improving visual function in glaucoma patients. Is there functional reorganization in primary visual cortex in response to glaucoma in human? If the emergence of degradation of visual fields takes a few months of sustained elevated IOP in rats and it happens when ganglion cell death cascade has slowed down, it might take much longer time in human where IOP in glaucomatous eye has been managed. Treating the visual centers by neuroprotective agents so that death of LGN and cortical neurons is reduced or controlled might benefit patients with glaucoma.

REFERENCES


