Research objectives

Glaucoma is the most common optic neuropathy characterized by progressive damage to the optic nerve and visual field limitations. The incidence of this disease increases with age. The most important trigger of the glaucomatous damage is elevated eye pressure and current standard approach in glaucoma therapy is reduction of the intraocular pressure. Untreated glaucoma ultimately leads to irreversible loss of vision. Despite of effective medications or surgical treatment leading to lowering of the intraocular pressure, progression of glaucomatous changes and loss of vision among glaucoma patients is common. It is critical to prevent vision loss through appropriate treatment. Pathophysiological mechanisms accompanying glaucoma are poorly understood, therefore undertaking the studies which may add significantly to the current knowledge on glaucoma impact on the visual system and influence the design and effectiveness of the therapeutic methods supporting current medication, is an urgent need. We plan to undertake the studies aimed to stimulate processes which lead to optic nerve neuroprotection and to maintenance of the normal activity of retinal cells and neurons in the visual cortex. Our aim is to estimate the efficiency and side effects of neurotrophic factor like brain-derived neurotrophic factor (BDNF) on the level of the retina and visual cortex and to investigate the outcome of experimental gene therapy in glaucoma through long-term enhancing of BDNF gene expression in the retina. The importance of BDNF supplementation in glaucoma is well documented in the animal studies. This positive results strongly argues for using similar method in glaucoma treatment. During accomplishment of our project we plan to elucidate pathophysiological mechanisms of glaucomatous changes in the visual cortex and to achieve knowledge about influence of increased level of BDNF on morphology of retinal ganglion cells (RGC) which relay visual information to higher brain structures and function of neuronal cells within higher levels of visual system in animals with glaucoma and animals from control group.

Research project methodology

To induce the level of BDNF in retina we plan to inject recombinant adeno-associated viral vectors (AAV) for BDNF (AAV-BDNF) into vitreal camera of the rat's eye. We will estimate positive and negative impact of increased BDNF level in the visual system structures, especially the influence of this neurotrophin on survival of retinal ganglion cells, and on the neuronal activity of visual cortex and subcortical visual structures. Present data with gene therapy in glaucoma treatment seems to be very promising, but there are also studies that proved that some AAV serotypes induce reactive astrocytosis, dysfunction of GABAergic network and development of dendritic trees of retinal ganglion cells. Excessive development of RGCs dendritic trees may lead to reduction of spatial resolution and reduction of visual acuity. We will use glaucoma model established by researchers from Medical University of Silesia to estimate glaucomatous pathophysiological changes and influence of BDNF on the retina and higher levels of visual system with retinal cells staining, optical imaging and electrophysiological techniques.

Expected impact of the research project on the development of science, civilization and society.
We expect that these results, if positive, will serve as a base for development of the new method for treatments of glaucoma and other retinal degenerative diseases in clinical practice. Our project should answer the question whether intraocular delivery of this neurotrophic factor is an efficient and safe method leading to its increased level within retinal tissue and neuroprotection of retinal ganglion cells impeding loss of vision.Our studies may also help to understand pathological mechanisms present in glaucoma patients within the higher level of visual system. Understanding of these mechanisms can be crucial for prevention of irreversible loss of vision in glaucoma patients.