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Editorial

Neuropeptide Research in the Eye

The neuropeptide research in the eye is the main topic of our scientific group in Innsbruck. Most of the neuropeptides have been discovered more than 30 years ago and the presence and distribution of some of them has been explored in the eye in the 80´s mainly by Richard Stone. This concerns particularly substance P (SP), calcitonin gene-related peptide (CGRP), vasoactive intestinal polypeptide (VIP) and neuropeptide Y (NPY). Whereas SP and CGRP have been found to be constituents of the sensory innervation of the eye, VIP is present in the parasympathetic and NPY in the sympathetic innervation of the eye. These results have been reviewed in 1987 in "Experientia". In the retina, the typical neuropeptide localization are amacrine cells in the proximal inner nuclear layer and displaced amacrine cells in the ganglion cell layer but some of them are also present in ganglion cells. As mentioned above the flowering time of the neuropeptide research in the eye were the 80´s because everyone believed that these are novel neurotransmitters apart from the catecholamines, acetylcholine and certain amino acids. But it came apparent that these are rather neuromodulators and probably because of this reason the interest in neuropeptide research decreased in the last three decades. However, the innervation of the eye by several further peptides has been explored including galanin, somatostatin, cholecystokinin, nitric oxide, pituitary adenylatecyclase (PACAP) and neurokinin A and the results of these explorations have been reviewed in the year 2007 by our scientific group in Innsbruck in "Brain Research Reviews" and in the book "Neuropeptides in the eye" which has been released in 2009 in "Research Signpost". Since then, further neuropeptides have been characterized in the eye. This concerns the chromogranin A-derived peptides WE-14, GE-25, catestatin and serpinin, the chromogranin B-derived peptide PE-11 and the secretoneurin II-derived peptide secretoneurin. The presence and distribution of most of these chromogranin-derived peptides has been explored by us and they have been found to be typical constituents of the sensory innervation of the eye as well.

Hence, the presence and distribution of several neuropeptides are well explored whereas their functional role is not clear and is not fully understood. The first functional role of neuropeptides in the eye has been found to be neurogenic inflammation in the eye which has mainly been explored in rabbits. This represents a response after topical irritation and consists of miosis which is mediated by SP and vascular effects which are accomplished by CGRP. Furthermore, PACAP and nitric oxide participate as well. On the other hand, several effects of neuropeptides have been found in the last three decades and consequently they might be involved in the pathophysiology of the eye. In particular, SP is definitely involved in the pathobiology of neurotrophickeratopathy, VIP in the promotion of survival of corneal endothelium under oxidative stress and certain peptides also in immune privilege in the ocular microenvironment. On the other hand, an involvement in aqueous humour dynamics, contraction or relaxation of the sphincter and dilator muscle and an influence of uveal blood flow have been described for certain peptides. There are three examples which should demonstrate that it is important to continue the neuropeptide research in the eye because they might be relevant clinically in ophthalmic diseases. Firstly, certain neuropeptides act proangiogenic and might thus be involved in neovascular diseases of the eye, in particular in retinopathy of prematurity, wet age-related macular degeneration, proliferative diabetic retinopathy and neovascularizations after central retinal vein occlusion. This concerns SP, NPY, secretoneurin and catestatin. Next, neuropeptides have been found to inhibit the proliferation of retinal pigment epithelial cells. This might be clinically relevant in proliferative vitreoretinopathy where these cells are swept out into the vitreous and begin excessively to proliferate. And finally, some neuropeptides act neuroprotectively on ganglion cells and inhibit death and loss of these cells under various pathologic manipulations. This is especially the case for PACAP and VIP. Since these peptides are present in the retina they might be involved in endogenous neuroprotection within the retina which would be clinically relevant in glaucoma.

In conclusion, it seems to be important to encourage scientists from the whole world to continue to explore on this scientific field because neuropeptides might be clinically more relevant in certain ophthalmic diseases than suggested so far. And the "Journal of Clinical Research and Ophthalmology" might be a novel platform for manuscripts dealing with this topic.

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