Proceedings of the British Pharmacological Society at http://www.pA2online.org/abstracts/Vol10Issue2abst017P.pdf

Differences between wild type and PACAP KO mice in adult and aging retina: neurochemical and ultrastructural analysis

Krisztina Szabadfi[1], Peter Kiss[2], Dora Reglodi[2], Andrea Tamas[2], Hitoshi Hashimoto[3], Zsuzsanna Helyes[4], Seiji Shioda[5], Robert Gabriel[1]. *[1]Department of Experimental Zoology and Neurobiology, University of Pecs, Pecs, Hungary, [2]Department of Anatomy, PTE/MTA Lendulet PACAP Research Team, University of Pecs, Pecs, Hungary, [3]Graduate School of Pharmaceutical Sciences, Osaka University, Osaka, Japan, [4]Pharmacology and Pharmacotherapeutics, University of Pecs, Pecs, Hungary, [5]Showa University, Tokyo, Japan*

Pituitary adenylate cyclase activating polypeptide (PACAP) is a neurotrophic and neuroprotective peptide. PACAP and its receptors are present in the retina. We have provided that PACAP is neuroprotective in retinal degenerations. Mice deficient in endogenous PACAP have a more severe retinal lesion in excitotoxic and ischemic injuries, suggesting that endogenous PACAP is part of the retinoprotective machinery. Therefore, the aim of this study was to examine whether histological alterations, cell type-specific differences or changes in the distribution of PAC1-R expression exist between the retinas of wild type and PACAP deficient mice in adult (3-5-months-old) and aging (1-year-old) animals. Retinas were processed for routine histology, electromicroscopical analysis and immunohistochemistry for TH, calretinin, calbindin, parvalbumin, PKCα, GFAP, PNA and PAC1-R.

Standard histological methods revealed no major differences between the adult retinas of wild type and PACAP deficient mice. Staining for the above markers of adult PACAP KO retinas was similar to that of wild type retinas, with no significant alterations in immunoreactivity patterns, except for PAC1-R staining. We observed that fewer cells expressed PAC1-R in adult PACAP KO than in wild type retinas. Among the age-related changes, the number of cone photoreceptor terminals was reduced in both wild type and PACAP KO aging retinas compared to adult controls. Other well-known age-related differences were, however, only observed in the PACAP KO mice. These alterations included: horizontal cell processes sprouted into the photoreceptor layer; bipolar cells showed arbor-specific alterations: their dendrites sprouted but their axons remained stable and Müller glial cells showed elevated GFAP expression compared to the aged wild type retinas. Ultrastructural differences were also revealed in the aging PACAP KO retinas, particularly in connection with synaptic contacts.

In summary, while there are no major differences in the histological structure and expression of markers between adult wild type and PACAP KO mice, there are marked degenerative changes that appear earlier in aging mice lacking endogenous PACAP. These results support the endogenous protective role of PACAP against aging processes of the nervous system.

Supported by OTKA K72592, K100144, CNK78480; Bolyai Scholarship; Richter Gedeon Centenary Foundation; PTE-MTA Lendület program, SROP-4.1.2.B-10/2/KONV-20/0-0002, SROP-4.2.2/B-10/1-2010-0029; Arimura Foundation.