AB027. Nogo-A neutralisation improves vision recovery after retinal injury

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Background: In glaucoma and after an ischemic injury of the retina, excessive activation of N-Methyl-D-Aspartate receptors, a type of glutamatergic receptors, induces the death of retinal ganglion cells and an irreversible vision loss. The painless loss of retinal cells does not allow for a swift diagnostic and treatment of retinal damages. There is no efficient therapy to improve retinal functions in this case. In order to develop new therapeutic approaches for retinal injury, we propose, in this study, to stimulate neuronal plasticity of the visual system by neutralising the glial protein, Nogo-A. The inhibitory action of this protein on axonal regeneration is well known in spinal cord injuries but not in the visual system. We thus studied the function of Nogo-A in vision recovery in mice.

Methods: Nogo-A activities were chronically blocked by deleting its gene in KO mice and acutely, by intravitreal injections of an antibody known as 11C7. Inner retina lesions were done by injection of 0.5 or 5 nmol of NMDA in the vitreous humor. A PBS buffer was administered in control animals. The visual system functions were accessed with an optokinetic test in awake mice, by electroretinography (ERG) in the eye and visual evoked potentials in the visual cortex. Cell survival of retinal ganglion cells, amacrine and bipolar cells was evaluated on histological sections by immunofluorescence. Changes in expression of Nogo-A, its receptors and neuronal plasticity associated molecules were observed by Western blot and q-PCR.

Results: At NMDA doses of ≤0.5 nmol, Nogo-A KO mice show a recovery of optokinetic responses much faster than in WT mice. Surprisingly, a single injection of the antibody, 11C7 was sufficient to improve VEPs of NMDA injured animals as compared to control antibody. Furthermore, ERGs showed that a dose of 0.5 nmol induced retinal lesions limited to the ganglion cell layer, with significant changes to the VEPs but without influencing photoreceptors and inner nuclear layer cells functions. However, 5 nmol of NMDA affected the survival of inner nuclear layer cells and reduced by ~50% their activity.

Conclusions: Our results show that the neutralisation of Nogo-A can improve visual functions after injury to the inner retina. Inhibition of Nogo-A could thus be an efficient way to treat pathologies like glaucoma.

Keywords: Optokinetics; visual evoked potentials; Nogo-A; 11C7

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