ALPHA-SYNUCLEIN ANTIBODIES REDUCE NEURODEGENERATION IN A GLAUCOMA ANIMAL MODEL

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Purpose: Glaucoma is a neurodegenerative disease including apoptosis of retinal ganglion cells (RGC) and axons. Altered serum autoantibody (Aab) levels occur in glaucoma patients. Beyond others, antibodies (Ab) to α-synuclein have been identified. Aim of the study is to unravel the mode of action of α-synuclein Ab.

Methods: Intraocular pressure (IOP) was elevated in Sprague Dawley rats (n=14) by episcleral vein occlusion. Intravitreal injection (IVI) was performed after IOP rise. Fellow eyes served as (1) normotensive controls (n=14) and were compared with IOP elevated eyes of (2) controls (n=3, no IVI), (3) buffer (n=6, IVI of buffer), (4) α-synuclein Ab (n=5, IVI of 25 µg α-synuclein antibody). Optic nerves and retinae were collected for PPD- and Brn3a staining. Retinal tissue was used for ESI-MS/MS analysis. Results: Episcleral vein occlusion increased IOP significantly to 17.8±1.1 mmHg compared to fellow eyes with 11.3±0.4 mmHg (p<0.01). Axon density/mm² showed a decay to 322477±37055 (p<0.01) in controls, 307787±28399 (p<0.01) in buffer group, and 399818±16529 (p=0.19) in the α-synuclein Ab group compared to fellow eyes with 439529±18161 axons/mm². The RGC density/mm² was reduced to 1076±132 (p<0.05) in controls, 1068±163 (p<0.01) in buffer group and 1252±95 (p=0.08) in α-synuclein Ab group compared to fellow eyes with 1516±186 RGC/mm². Mass spectrometric analysis revealed upregulated levels of peripherin-2 (240x) and cofilin-1 (350x) in α-synuclein Ab group. Conclusions: Decreased neurodegeneration was found in α-synuclein Ab group. Peripherin-2, an intermediate filament and cofilin-1, an actin-binding protein reorganizing actin filaments, are upregulated. This indicates a cytoskeletal reorganisation, leading to an improved neuronal survival.