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View Abstract

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Commercial Relationships Disclosure: Annie Ryan: Commercial Relationship: Code N (No Commercial Relationship) | Tyler Heisler-Taylor: Commercial Relationship: Code N (No Commercial Relationship) | Matthew Reilly: Commercial Relationship: Code N (No Commercial Relationship)

Study Group: (none)

ABSTRACT

TITLE: Therapeutic Intervention in a Glial Stress Correlated Functional Deficit Small Animal Model of Traumatic Optic Neuropathy

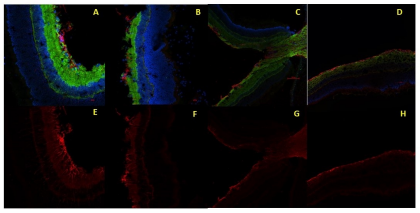
ABSTRACT BODY:

Purpose: Traumatic optic neuropathy (TON) is a vision loss disorder which arises after head injury. Diagnostic criteria and treatments are limited, due to a lack of translational animal models. We developed a diagnostic protocol utilizing electroretinograms (ERGs) in a small animal (rat) model of a torsion-induced TON which produced a deficit in photopic negative response (PhNR) after one week (D7). Here, we investigated molecular markers of glial stress arising post injury and therapeutic diffusion into the retina and optic nerve.

Methods: Male rats (~200g) were used for both glial stress (n=14; Sprague Dawley) and therapeutic (n=14; Long Evans) characterization. *Glial Stress:* Right eyes of 10 animals (+4 shams) were injured; retinas and optic nerves were retrieved for histological comparisons using β-tubulin, glial fibrillar acid protein (GFAP), and DAPI at D7. *Therapeutics:* ibudilast, Tauroursodeoxycholic acid (TUDCA), cyclosporine, and Anakinra were administered via retrobulbar (RB) and intravitreal (IVT) injections. Retinas and optic nerves were collected for mass spectrometry and proteomic evaluation.

Results: GFAP labeling was increased at D7, suggesting the presence of retinal stress. Correlating with significantly altered PhNR amplitudes occurring in the injured eyes, confirming our model inflicts TON. Cyclosporine was detected in both the retina (IVT: 383 ppb; RB: 16ppb) and optic nerve (IVT: <5ppb; RBB: 49ppb). TUDCA and ibudilast were not detected in either the retina or optic nerve via either injection route.

Conclusions: GFAP labeling increased in injured eyes indicates stressed retinal conditions and hypertrophic Müller cells. It is crucial to determine a therapeutic capable of reaching the posterior segment. We determined cyclosporine may be the optimal therapeutic as both RB and IVT injection methods observed measurable concentrations of therapeutic at target areas 24 hours after injection. This work was partially funded by US Department of Defense Vision Research Program Award W81XWH-15-1-0074 and the OSU Vision Sciences Research Core Program (OSU-VSRCP, P30EY032857). The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.



Retina/Optic nerve fluorescent image. Injured (A,C,E,G); Contralateral (B,F); Sham (D, H).

DETAILS

PRESENTATION TYPE - PLEASE NOTE, IF YOU CHANGE YOUR PRESENTATION TYPE AFTER APPLYING FOR AN AWARD (BELOW), YOU MUST GO BACK AND RESELECT THE APPLY BUTTON.: #1 Paper, #2 Poster

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TRAVEL GRANTS and AWARDS APPLICATIONS

AWARDS: ARVO Members-in-Training Outstanding Poster Award|ARVO and ARVO Foundation Travel Grants