Establishing an *in-vivo* retinal edema model in the chick

Posterboard#: B0395

Abstract Number: 806 - B0395

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Purpose

The chick (*Gallus gallus*) is very useful for ocular research due to its low cost, cone-rich retina. Similar features to the human macula make it promising for the development of an *in vivo* retinal edema model. The N-methyl-D-aspartate (NMDA) excitotoxic damage model has similarities to retinal vein occlusion and causes significant retinal edema and subsequent death of inner retinal neurons one day post-injury. Vascular endothelial growth factor (VEGF) has been shown to be critical in the development of retinal edema in human and other animal models. Aquaporin-4 (AQP4) is a water channel protein thought to play a role in retinal edema. We aim to develop a VEGF-induced chick edema model and compare it to the NMDA model.

Methods

Following an IACUC-approved protocol, chicks (n=12) were injected intravitreally with a dose of VEGF equivalent to that used in other animal models of blood retinal barrier disruption (0.2µg/20µl) compared to saline (vehicle) (n=16). Spectral domain optical coherence tomography (SD-OCT) retinal layer thickness measurements were performed on chicks at Day 1 (D1) and Day 7 (D7). The VEGF model data were compared with database measurements of NDMA (500nmol/20µl in one eye and saline vehicle in the fellow eye, n=10). AQP4 was assessed using immunohistochemistry on D1 and D7 through measuring the mean intensity in the inner retina and quantitation using NIS-Elements. TUNEL cell death staining was performed on D1 eyes. Data were analyzed using one-way ANOVA with Tukey and Sidak HSD post-hoc testing with GraphPad PRISM software.

Results

NMDA caused significant retinal edema at D1 as measured by total retinal thickness (NMDA: 344.7±5.676µm vs Saline: 279.6±5.459µm, p= <0.0001). There was no significant difference with VEGF on D1 and D7. TUNEL levels in NMDA-treated eyes had significantly higher number of cell death (3624.94±449.51 vs 0.00±0.00 TUNEL positive cells/mm^2, p=0.0211 vs untreated). VEGF did not lead to cell death as indicated by negative TUNEL staining(0.00±0.00 TUNEL positive cells/mm^2). NMDA AQP4 expression on D1 was increased in the inner nuclear layer in comparison to VEGF and control (NMDA: 54.03±15.638mean intensity/pixels^2 vs Saline: 25.54±1.468,p=<0.0036; vs VEGF:24.90,p=<0.0030).

Conclusions

NMDA injection induces significant retinal edema in the chick, while VEGF injection does not. The avascularity of the chick retina may play a role in the absence of VEGF-induced retinal edema.