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View Abstract

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AUTHORS

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Commercial Relationships Disclosure: Evan Hawthorn: Commercial Relationship: Code N (No Commercial Relationship) | Tyler Heisler-Taylor: Commercial Relationship: Code N (No Commercial Relationship) | Sandeep Goswami: Commercial Relationship: Code N (No Commercial Relationship) | Colleen Cebulla: Commercial Relationship: Code N (No Commercial Relationship)

Study Group: (none)

ABSTRACT

TITLE: Title: Changes in Morphology and Distribution of Microglia Following MIF Inhibition in Avian Excitotoxic Retinal Damage

ABSTRACT BODY:

Purpose: Purpose: Noxious insult to the retina triggers microglia activation that manifests as an amoeboid morphology and migration to the site of injury. Inhibition of macrophage migration inhibitory factor (MIF) has shown to be protective in excitotoxic retinal damage models. We evaluated the effects of MIF inhibition on microglia morphology and distribution in the retina following N-methyl-D-aspartate (NMDA) damage, which simulates glutamate excitotoxicity involved in retinal ischemic disease.

Methods: Methods: Under an IACUC-approved protocol, white leghorn chicks were treated with intravitreal injections (20ul) of NMDA (500nmol) + Ibudilast (1mg/ml) in the left eye, and NMDA (500nmol) + vehicle (sterile saline) in the right eye. Chicks were sacrificed at one-day post-injection (D1) (n=6), or nine days post-injection (D9) (n=8). Microglia were evaluated using CD45 immunohistochemistry. D1 images were analyzed using ImageJ to calculate the average mean intensity and area above a threshold. D9 Images were analyzed using NIS-Elements software. To investigate differences in microglia distribution, the retina was divided into three layers: Photoreceptor + Outer Nuclear Layer (PR-ONL), Outer Plexiform Layer + Inner Nuclear Layer (OPL-INL), and Inner Plexiform Layer + Ganglion Cell Layer + Nerve Fiber Layer (IPL-GCL-NFL). The area, form factor 1 (FF1), aspect ratio (AR), and cell count were measured for each cell identified through thresholding the CD45 signal. Statistics were performed in JMP with the Wilcoxon 2-sample test.

Results: Results: In the D1 group, microglia were solely located in the inner plexiform layer (IPL) 24h after damage in both treated and control groups. There were no significant differences in CD45 intensity (p=0.82) or area above a threshold (p=0.45). In the D9 group the count of CD45 positive macrophages decreases with Ibudilast treatment (16.69 vs. 9.31, p=0.029) in the PR-ONL layer. All other measurements in all three layers were not found to exhibit significant differences.

Conclusions: Conclusion: The decrease in microglia in the photoreceptor layer may indicate that Ibudilast treatment inhibits MIF’s ability to bind to CCR4, thereby reducing microglial migration to the inner retina. Further studies involving additional markers are required to fully elucidate the effect of Ibudilast treatment on microglia dynamics and activation.

(No Image Selected)

DETAILS

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TRAVEL GRANTS and AWARDS APPLICATIONS

AWARDS: