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Morphological, functional, and behavioral alterations in a microbead-induced mouse glaucoma model

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Purpose

Glaucoma is a neurodegenerative disease characterized by increased intraocular pressure (IOP), leading to retinal ganglion cell (RGC) loss and vision impairment. The main aim of the study was to examine the correlation of ocular hypertension with morphological, functional and behavioural parameters in the mouse magnetic microbead glaucoma model.

Methods

Elevated IOP was induced in 10-week-old male C57BL/6JRj mice (N=14) through intracameral unilateral injection of magnetic microbeads on Day 0. IOP was monitored using the Tonolab rebound tonometer up to Day 31 post-induction. On week 4 post-induction, spectral-domain opticalcoherence tomography (SD-OCT) imaging was performed to quantify the inner retinal thickness (INL). Pattern electroretinography (pERG) was recorded to assess retinal ganglion cell function. In addition, visual acuity (VA) and contrast sensitivity (CS) were evaluated on Day 31. On the same day mice were sacrificed, retinas were collected for retinal ganglion cells immunostaining with anti-RBPMS antibody and quantification of RBPMS-positive cells using stereology.

Results

IOP was significantly elevated by Day 3 as compared to contralateral eyes (17.6 ± 1.3 vs. 10.1 ± 0.1 mmHg) and remained significantly elevated throughout the whole follow-up period of 31 days. On Day 31, INL thickness was significant decreased in microbead-injected eyes as compared to naïve mice (85.7 ± 3.7 vs. 97.6 ± 0.5 µm, respectively, P<0.001). Similarly, microbead-injected eyes had significantly decreased pERG amplitude (2.4 ± 0.6 vs. 6.0 ± 1.0 µV, P=0.007) as compared to naïve animals. Furthermore, a significant impairment was observed in both optomotor reflex parameters VA (0.178 ± 0.038 vs. 0.389 ± 0.001 cycles/°, P<0.001) and CS (52.0 ± 16.5 vs. 8.4 ± 0.7 %, P=0.03) in microbead-injected eyes as compared to naïve animals. The number of RBPMS-positive cells decreased by 28% in the microbead-injected eyes as compared to healthy contraletaral eyes (2192 ± 102 vs. 3040 ± 69 cells/mm, P<0.001). Cumulative IOP showed no significant correlation with INL thickness, OMR measurements or RBPMS-positive cell numbers, but significantly correlated with pERG amplitudes (r = -0.7545, P<0.005).

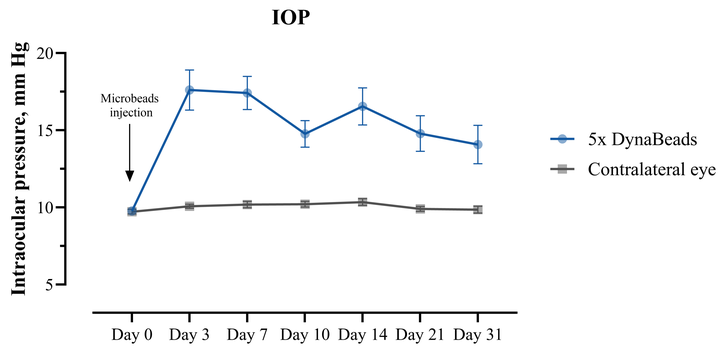


Figure 1. Intraocular pressure values throughout study period. Data are presented as mean ± SEM.

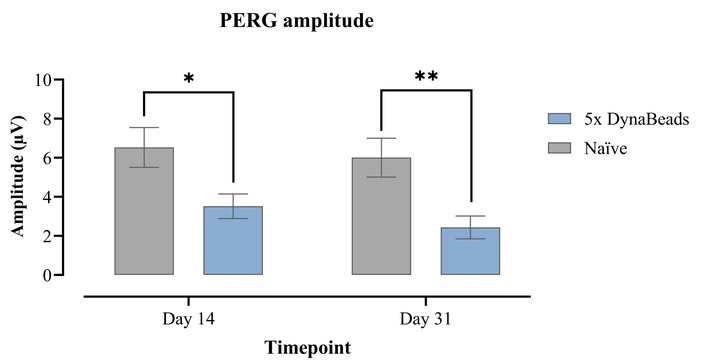


Figure 2. PERG amplitudes throughout study period. Data are presented as mean ± SEM and were compared by unpaired t test, * *P* < 0.05, ** *P* < 0.005.

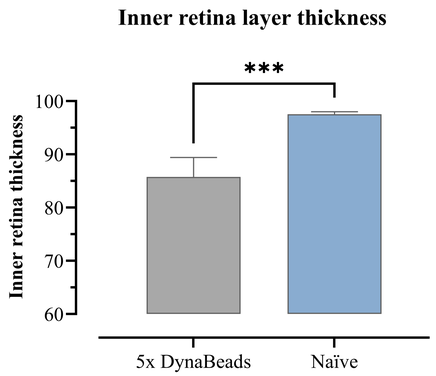


Figure 3. Inner retina layer thickness at different timepoints. Data are presented as mean ± SEM and were compared by unpaired t test, *** *P* < 0.005.

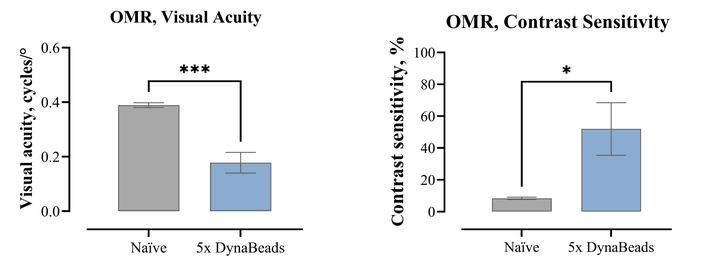
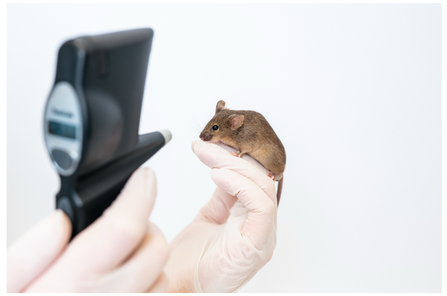


Figure 2. Optodrum VA and CS values throughout study period. Data are presented as mean ± SEM and were compared by unpaired t test, * *P* < 0.05, ** *P* < 0.005.

Conclusion

Cumulative IOP has a significant correlation with RGC function in the magnetic microbead-injected mouse model.



Disclosures
KM, TP, UB, JU, IL: none
SR: Experimentica Ltd. (I,S)
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