Characterization of a mouse model of age-related macular degeneration (AMD) generated by laser-induced choroidal neovascularization and pharmacological improvement by aflibercept

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Background

Age-related macular degeneration (AMD) is a medical condition in which damage in the macula of the retina results in blurred or loss of vision. Out of the two types of AMD, dry and wet, wet AMD is responsible for 90 % of AMD-associated vision loss. Wet AMD is caused by abnormal expression of vascular endothelial growth factor (VEGF) that results in choroidal neovascularization, which in turn disturb the retinal pigment epithelium (RPE) layer, damaging photoreceptors and leading to vision loss.

The objective of this study was to evaluate the therapeutic effect of aflibercept (Eylea™, Bayer, Germany) in a mouse model of laser-induced choroidal neovascularization (CNV). In addition to measuring lesion size, mouse behavior was observed in the home cages, using the Home Cage Analysis (HCA) system (Actual Analytics, UK).

METHODS

Model generation and treatment

- Male C57BL/6 mice at 8 weeks of age were anesthetized, and one drop of Mydriacyl eye drop (tropicamide) was applied to each eye for mydriasis.
- 3 laser spots (200 mW, 50 µm spot size, 100 ms duration) were applied around the optic nerve head using a 532 nm laser device (Iridex Oculight Tx, USA) attached to a slit lamp.
- Aflibercept was diluted to 2 mg/ml in filtered 1XPBS. 1.5 µl of aflibercept or vehicle (1XPBS) was injected intravitreally after model generation.

Optical coherence tomography (OCT)

- OCT and fluorescein angiography (FA) were performed 8 and 14 days after model generation using the Heidelberg Spectralis HRA + OCT device (Heidelberg, Germany). A 78D condensing lens (Volk Optical, USA) was taped in front of the camera.
- FA images were taken 10 minutes after injection of fluorescite 10% (Alcon, USA).

Home cage analysis (HCA)

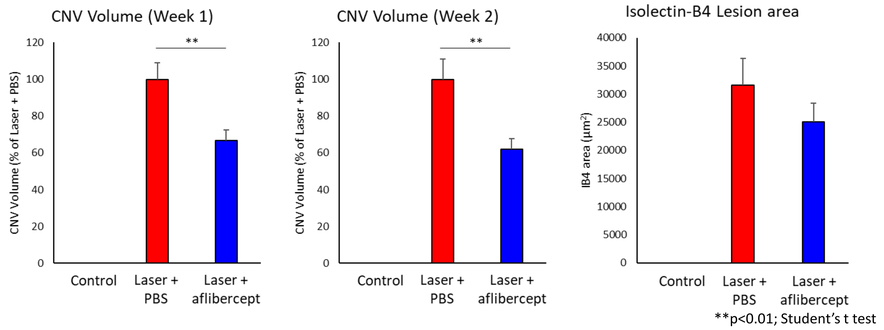
- After laser model generation and treatment, RFID chips were inserted subcutaneously in the abdomen.
- Mice were housed in their home cages that were slotted inside the HCA apparatus, which consists of a baseplate RFID reader under the cage that records positional information, and an infrared HD video camera for continuous recording.
- Locomotor activity and social interactions in the home cage were recorded and analyzed.

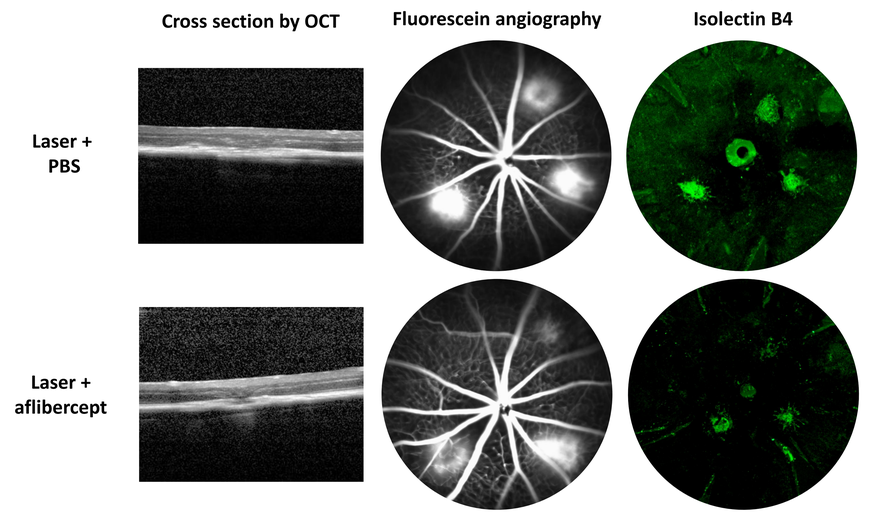
Histology

- 20 days after model generation, the eyecups were collected and flatmounted.
- The choroidal flatmounts were stained with Isolectin B4 antibody.

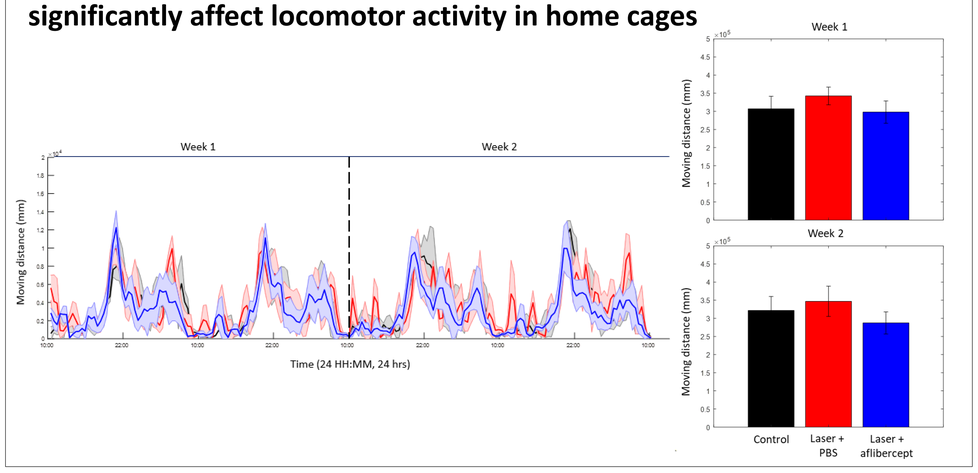
RESULTS

1. Treatment with aflibercept reduced CNV size



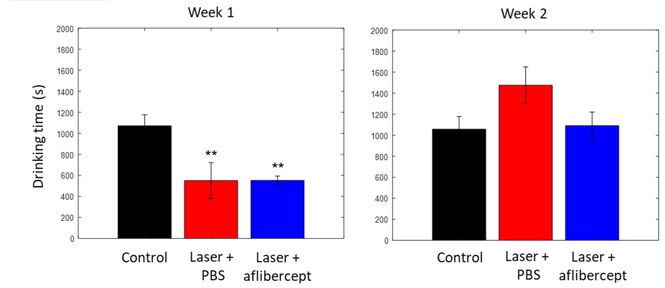


2. Laser induced CNV and treatment with aflibercept did not significantly affect locomotor activity in home cages

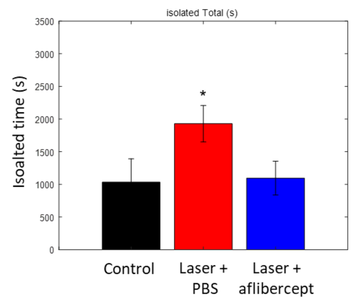


3. Laser induced CNV affected mouse behavior in home cages

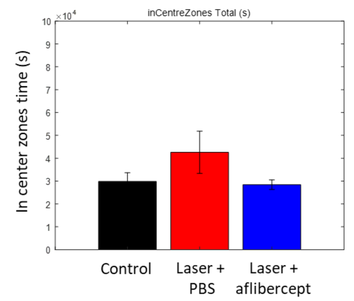
Drinking time



Isolated time (Week 2)



In center zones time (Week 2)



*p<0.05, **p<0.01; vs Control, LSD post-hoc test

CONCLUSIONS

1. **Treatment with aflibercept significantly reduced CNV volume when observed *in vivo* using OCT, 1 and 2 weeks after laser model generation.**
2. **Treatment with aflibercept reduced area of Isolectin-B4 staining in choroidal flatmounts 20 days after laser model generation.**
3. **Locomotor activity in home cages was generally not significantly affected by the laser model and treatment with aflibercept compared with the control group (no laser).**
4. **Laser groups showed reduced drinking time compared with the control group 1 week after laser model generation. This was not observed 2 weeks after laser model generation.**
5. **2 weeks fater laser model generation, laser + PBS groups showed higher isolated time and in center zones time compared with the control and laser + aflibercept groups.**