Neuroprotective Effects of a Novel ROCK inhibitor in a Rat Model of Anterior Ischemic Optic Neuropathy

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Purpose

Anterior ischemic optic neuropathy (AION) is ischemic damage to the optic nerve causing retinal ganglion cell death. Currently there is no effective treatment. The Rho-associated kinase (ROCK) is known to trigger oxidative stress, causing cell death. We use a novel ROCK inhibitor (E212) in this study to investigate the RGC survival and visual function in the experimental AION.

Methods

1. **The rats immediately received an intravitreal injection of either E212 or PBS after AION induction**
2. **The visual function was assessed by flash visual evoked potentials (FVEP)**
3. **Retrograde of fluorogold were used to labelling retinal ganglion cells (RGCs).**
4. **To determined the reactive oxidative stress (ROS) in RGCs, we used CellROX assay.**
5. **To determined the macrophage infiltration into optic nerve (ON), immunohistochemistry of ED1 were performed.**
6. **To evaluated the distribution of tight-junction protein in ON vessels, immunohistochemistry of ZO-1 were performed.**
7. **Superoxide dismutase (SOD) activity in ONs was performed using SOD activity ELISA kit.**

Results

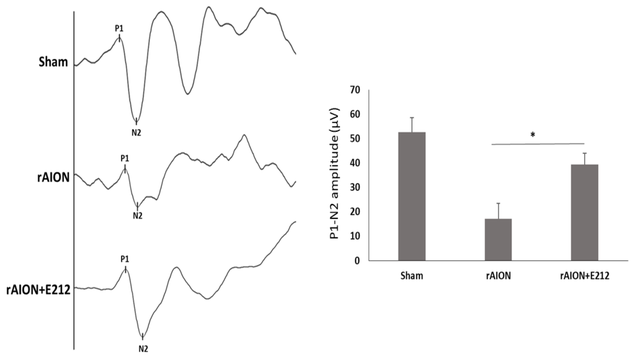

Fig. 1. FVEP after E212 treatment. The P1-N2 wave shows a significantly improved in the E212 treatment group compared to rAION PBS group. (Sham 53±6 μV, rAION 17±6 μV, E212 39±4 μV, n=6, p<0.05).

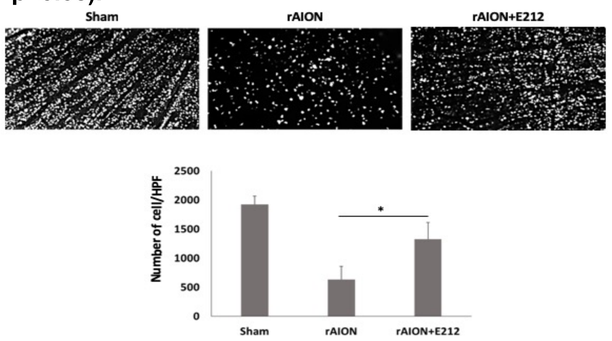

Fig. 2. Flat-mounted central retinas and the morphometry of RGCs in each group. The RGC density is significantly improved by 48% in the E212 treatment group compared to rAION PBS group. (Sham 1923±143 cells, rAION 645±220 cells, E212 1319±160 cells, n=6, p<0.05).

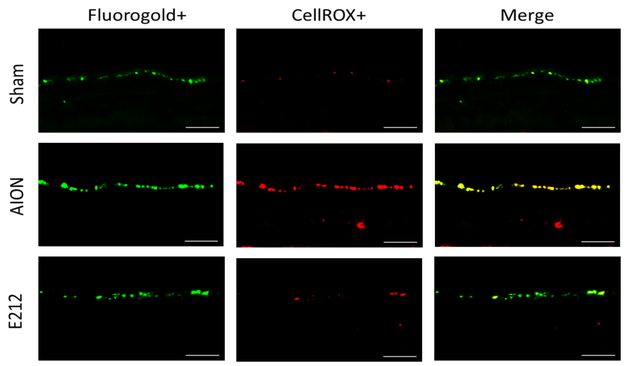

Fig. 3. Fluorogold labelled RGCs and CellROX labelling ROS producing cells. CellROX labelling shows the number of the ROS-producing cell in RGC layer was less in the E212-treated group than those of PBS-treated group.

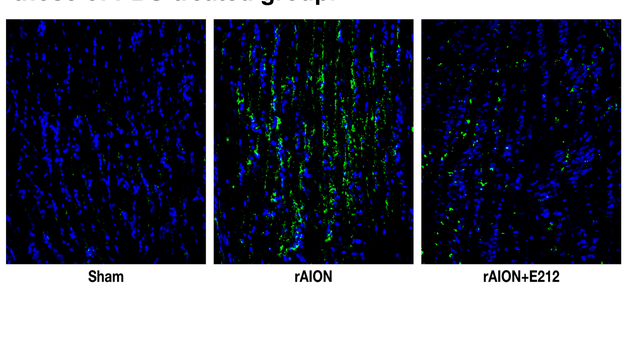

Fig. 4. ED-1 staining shows in E212 group ED-1 positive cells were reduced compared to PBS-treated group.

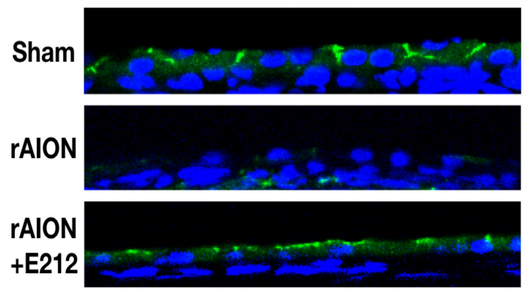

Fig. 5. ZO-1 staining for RPE tight-junction integrity. E212 treatment inhibited the disruption of blood-retinal barrier after 3 days ON infarct compared to PBS treatment.

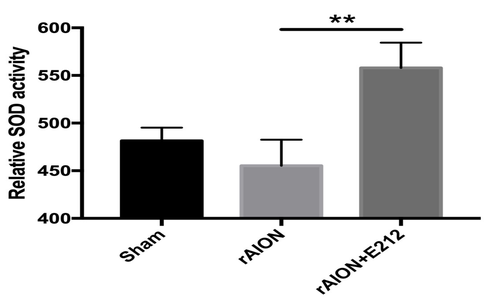

Fig. 6. Optic nerve 3 days after rAION induction for evaluation of anti-oxidation activity. SOD activity of ON is increased in the E212-treated group compared to those of PBS-treated group, suggesting E212 increase anti-oxidative activity (n=6).

Conclusion

1. **Treatment with E212 can preserve visual function in the rAION model compared to PBS treatment.**
2. **Treatment with E212 can rescue more RGCs after ON infarct compare with PBS treatment.**
3. **Treatment with E212 can reduce RGC oxidative stress after rAION induction.**
4. **Treatment with E212 can reduce ON infract and increase anti-oxidation activity compare to PBS treatment.**
5. **Treatment with E212 can rescue barrier tight junction breakdown compare to PBS treatment group**
6. **E212 has neuroprotective effects in the rAION model.**

References

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Disclosure

There are no financial conflicts of interest to disclose.

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