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Pharmacological inhibition of nitric oxide increases myopia susceptibility in mice

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Abstract

Purpose : Nitric oxide (NO), a gaseous neurotransmitter is synthesized in the mammalian retina and the choroid by activation of the enzyme nitric oxide synthase (NOS). Studies on chickens and guinea pigs have suggested that NO may mediate inhibition of axial eye growth through choroidal thickening. We hypothesize that pharmacological inhibition of NO will lead to myopic eye growth, thinner choroids and increased susceptibility to form-deprivation (FD) myopia in C57BL/6J wild-type mice.

Methods : Mice were treated with L-NAME (100-140 mg mixed with 100 ml of drinking water) beginning at postnatal day 10; control mice received normal drinking water. Refractive development was measured every 2 weeks from 4 to 14 weeks of age. Weekly measurements were performed on a separate cohort of mice that underwent monocular FD in the right eye from 4 weeks of age using head-mounted diffuser goggles. Refraction and ocular biometric measurements were obtained using photorefraction and spectral-domain optical coherence tomography.

Results : At 4 weeks, under unrestricted visual conditions, L-NAME treated mice (n=10) had similar refractive errors to control mice (n=10) (mean refractive error, L-NAME: +2.96 ± 0.31 D; control: +3.31 ± 0.40 D, $p>0.05$). However, L-NAME-treated mice became relatively more myopic than control mice at 6 weeks and remained relatively myopic thereafter (mean refractive error at 10 weeks, L-NAME: +4.52 ± 0.55 D, control: +6.06 ± 0.26 D, $p<0.05$). L-NAME mice exhibited significantly longer axial length compared to control animals (average across all ages, L-NAME: 3.25 ± 0.007 mm; control: 3.21 ± 0.01 mm, $p<0.05$). During development, L-NAME-treated animals (0.033 ± 0.002 mm) on average had significantly ($p<0.05$) thinner choroids than those of control animals (0.039 ± 0.002 mm). After 3 weeks of FD, goggled L-NAME mice (n=6) showed a significantly

greater myopic shift (difference between the right and left eyes) of -4.49 ± 0.84 D compared to goggled control animals (n=8, -2.81 ± 0.43 D, $p<0.05$). There were no significant changes in the axial lengths of either treatment group with FD.

Conclusions : Our findings suggest that pharmacological inhibition of NO significantly enhances the susceptibility to myopia under both unrestricted and FD visual conditions in mice. Future studies are needed to determine the contributions of specific NOS isoforms in this signaling process.

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