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Ascorbic acid, and not L-DOPA, protects against form-deprivation myopia in retinal degeneration mouse models.

Erica Landis; Hanna Park; Ranjay Chakraborty; Curran Sidhu; P. Michael Iuvone; Machelle T Pardue

+ Author Affiliations & Notes

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Abstract

Purpose : Mouse models of retinal degeneration have shown increased susceptibility to form deprivation myopia, potentially due to decreased dopamine (DA) turnover (Park *et al*., 2013) or loss of dopaminergic amacrine cells (DACs; Ivanova *et al*., 2015). The purpose of this work is to test whether systemic injections of the DA precursor, L-3,4-dihydroxyphenylalanine (L-DOPA) will protect against form deprivation (FD) myopia in wild-type and retinal degeneration mice.

Methods : Susceptibility to FD myopia was measured beginning at post-natal day 28 (P28) in $Pde6b^{rd10/rd10}$ (*rd10*) mice and age-matched C57BL/6J wild-type (WT) mice. A subset of animals was given monocular FD lenses following baseline measurements. At P28, mice received daily systemic injections of L-DOPA only (n=17), L-DOPA + the vehicle, ascorbic acid (AA)(n=18-25), or AA only (n=18-21). Weekly measurements of refractive error, corneal curvature, and ocular biometry were performed until P42, using photorefraction, keratometry, and spectral-domain optical coherence tomography. At P44 retinas were collected to measure dopamine (DA) and its metabolite 3,4-dihydroxyphenylacetic acid (DOPAC) with HPLC.

Results : WT mice exposed to FD developed a significant myopic shift (right-left eye) with AA only treatment (-3.54 ± 1.14D); that was significantly decreased by L-DOPA + AA (0.283 ± 0.588D, $p<0.01$). *Rd10* mice showed the opposite response such that AA only treatment significantly reduced the myopic shift in response to FD (-0.769 ± 0.464D) compared to L-DOPA + AA (-3.206 ± 0.734) or L-DOPA only treatments (-5.752 ± 0.761D, $p<0.05$). No significant changes were seen in corneal curvature or ocular parameters.

Conclusions : Similar to findings in other animals, L-DOPA treatment protects WT mice from FD myopia. However, L-DOPA treatments did not halt or slow FD myopia in *rd10* mice, while AA only treatments completely eliminated the myopic shift. We hypothesize that L-DOPA is not protective effect in rd10 mice due to dysfunctional DACs that aren't able to convert L-DOPA to DA. Furthermore, the anti-oxidant effects of AA on extracellular DA (Neal *et al*., 1999) may preserve DA in *rd10* retinas that is not rapidly degraded by defective DACs. We will confirm this hypothesis with the measurement of dopamine and DOPAC levels with HPLC in each treatment group.

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