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Eliminating the Master Clock Gene in the Murine Retina Produces Myopia

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Abstract

Purpose : BMAL1 is a transcription factor that is essential to the operation of the circadian clock mechanism in all tissues of the body, including the retina. Previous studies with chicks have linked intrinsic retinal circadian rhythms to experimental myopia (Stone et al., 2013). In this study, Cre-mediated, retinal specific BMAL1 knockout (KO) mice were examined to determine whether the BMAL1 gene and, by inference, circadian rhythms have a role in normal refractive development of the eye.

Methods : KO mice were on a C57BL/6J background and were homozygous for both the Chx10 Cre-recombinase and floxed Bmal1 alleles. Refractive development of KO (n=7) and age-matched wild-type (WT, n=10) mice were measured every 2 weeks from post-natal day 28 (P28) to P112 under normal laboratory visual conditions. Measurements of refractive error, corneal radius of curvature, and ocular biometric parameters were collected using an automated photorefactor, keratometer, and spectral-domain optical coherence tomography (SD-OCT) system, respectively.

Results : Under normal visual conditions, KO mice were significantly more myopic than WT mice throughout the developmental period (at P70: KO -0.413 ± 0.80 D; WT +4.81 ± 0.90 D; $p<0.001$). KO mice had longer axial lengths than WT mice (at P70: KO +3.24 ± 0.02 mm; WT +3.21 ± 0.01 mm; $p=0.007$). KO mice also showed shorter anterior chamber depths (at P70: KO +0.37 ± 0.003 mm; WT +0.38 ± 0.002 mm; $p=0.01$) and longer vitreous chambers (at P70: KO +0.61 ± 0.003 mm; WT +0.57 ± 0.002mm; $p<0.001$) than the WT mice. There were no significant differences in corneal curvature between KO and WT animals.

Conclusions : Our results indicate that Bmal1 is important for normal refractive development of the eye in mice. Future studies are needed to examine underlying mechanisms causing myopic refractive errors in Bmal1 KO mice and to evaluate the response of Bmal1 KO mice to modified visual input.

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