

What ocular components underlie the inhibition of myopia or hyperopia by glucagon or its antagonist?

X. Zhu, M.P. Feldkaemper*, J.A. Winawer, T. Park and J. Wallman. Dept. of Biology, City College, CUNY, New York, NY and *University Eye Hospital, Tübingen, Germany

Purpose: Glucagonergic amacrine cells show increased ZENK expression and increased glucagon mRNA content when positive, but not negative, lenses are worn (Feldkaemper et al., 2000; Fischer et al., 1999). Exogenous glucagon or its antagonist decrease experimental myopia or hyperopia, respectively (Feldkaemper et al., 2000; Stell et al., 2000). What ocular components underlie these effects?

Methods: Chicks wore either positive or negative spectacle lenses or diffusers over both eyes for 2 days; those wearing negative lenses or diffusers had one eye injected daily with 20 μ L of glucagon (10^{-4} M); those wearing positive lenses were injected with 20 μ L of a glucagon antagonist (des-His¹-(Glu⁹)-glucagon-amide, 14 μ M). Fellow eyes were injected with 20 μ L of saline. Axial dimensions were measured by A-scan ultrasonography.

Results: **1.** Glucagon completely prevented the choroidal thinning normally caused by wearing negative lenses or diffusers (glucagon vs. saline, change over 2 days, ANOVA, $p < 0.001$): diffusers: 158 μ m vs. -61 μ m; -7 D lenses: 47 μ m vs. -105 μ m; -15 D lenses: 2 μ m vs. -41 μ m. Glucagon partially inhibited the associated ocular elongation as well (ANOVA, $p < 0.05$): diffusers: -38 μ m vs. 16 μ m; -7 D lenses: -77 μ m vs. 36 μ m; -15 D lenses: -26 μ m vs. 83 μ m. **2.** The antagonist reduced the inhibition of ocular elongation normally caused by positive lenses in one of our conditions (antagonist vs. saline, paired 1-tailed *t*-test): +7 D lenses: -64 μ m vs. -125 μ m, $p < 0.05$; +15 D lenses: 20 μ m vs. -11 μ m, $p > 0.05$, but had no effect on the associated choroidal expansion (antagonist vs. saline, ANOVA, $p > 0.05$): +7 D lenses: 150 μ m vs. 103 μ m; +15D lenses: 261 μ m vs. 248 μ m.

Conclusions: The stronger effect of glucagon on the response to negative lenses was on the choroid. The only effect of the antagonist on the response to positive lenses was on the ocular elongation. Control experiments with drugs without lenses showed a similar trend. These two of the four ocular responses to positive and negative lenses were the same ones elicited by brief and infrequent episodes of lens-wear (Winawer et al., 1999).

Support : NIH EY02727, RR03060