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Adaptive Calibration of Dynamic Accommodation—Implications for Accommodating Intraocular Lenses

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Abstract

PURPOSE—When the aging lens is replaced with prosthetic accommodating intraocular lenses (IOLs), with effective viscoelasticities different from those of the natural lens, mismatches could arise between the neural control of accommodation and the biomechanical properties of the new lens. These mismatches could lead to either unstable oscillations or sluggishness of dynamic accommodation. Using computer simulations, we investigated whether optimal accommodative responses could be restored through recalibration of the neural control of accommodation. Using human experiments, we also investigated whether the accommodative system has the capacity for adaptive recalibration in response to changes in lens biomechanics.

METHODS—Dynamic performance of two accommodating IOL prototypes was simulated for a 45-year-old accommodative system, before and after neural recalibration, using a dynamic model of accommodation. Accommodating IOL I, a prototype for an injectable accommodating IOL, was less stiff and less viscous than the natural 45-year-old lens. Accommodating IOL II, a prototype for a translating accommodating IOL, was less stiff and more viscous than the natural 45-year-old lens. Short-term adaptive recalibration of dynamic accommodation was stimulated using a double-step adaptation paradigm that optically induced changes in neuromuscular effort mimicking responses to changes in lens biomechanics.

RESULTS—Model simulations indicate that the unstable oscillations or sluggishness of dynamic accommodation resulting from mismatches between neural control and lens biomechanics might be restored through neural recalibration.

CONCLUSIONS—Empirical measures reveal that the accommodative system is capable of adaptive recalibration in response to optical loads that simulate effects of changing lens biomechanics.

The progressive age-related loss of accommodative ability (presbyopia) can be primarily attributed to the increased stiffness of the crystalline lens.^{2,3} Currently, there is a major effort in the field of refractive surgery to restore accommodation in presbyopes by replacing the biological lens with prosthetic lenses that have structural designs and materials whose effective viscoelastic properties are lower than those of the biological lens (accommodating intraocular lenses [IOLs]).^{4,5} Most of these lenses are implanted in the capsular bag and they have different designs, including injectable polymers that mold within the capsular bag,⁶⁻⁸ axially translating lenses that increase the power of the eye by moving closer to the cornea,⁹⁻¹¹ and lenses with

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a combination of compliant materials, with a translating component, that are fixated in the ciliary sulcus on top of the capsular bag.¹² Injectable polymer lenses have yet to become clinically available because of remaining challenges of surgical procedures and postoperative capsular opacification.^{8,13}

The viscoelasticity of injectable lenses is mainly determined by the intrinsic mechanical properties of the polymer, and the lenses are usually designed with more compliance and either higher or lower viscosity than the natural presbyopic lens.^{6,7} The effective elasticity (1/compliance) of the axially translating lenses is typically lower than that of the natural lens, mainly due to increased structural compliance of their hinge-like mechanism of action. The effective viscosity of dual-haptic translating lenses might be higher than that of the natural lens due to viscous drag of lens movement within the fluid in the lens bag and anterior chamber.¹⁰ Evaluation of these lenses has been limited to subjective measures of accommodation amplitude and near visual acuity, both of which are likely to be influenced by the eye's depth of focus.^{4,5} Some objective measures of accommodation by the single-optic accommodating IOL (ICU A-IOL; HumanOptics AG, Erlangen, Germany) have been recorded, and these results generally show low or no accommodation following accommodating IOL implantation.¹⁴ There is scant, if any, objective assessment of the performance of these lenses in a dynamic negative feedback-driven environment.

The characteristics of blur-driven accommodation are typically determined by the biomechanics of the plant (crystalline lens, ciliary muscle, choroid, and zonules) and the neural signals that control the plant. Several observations suggest that the neural control of accommodation compensates for the age-related increase in viscoelasticity of the natural crystalline lens. For instance, the response AC/A ratio (the amount of vergence generated by a diopter of accommodation) increases^{15,16} and the response CA/C ratio (the amount of accommodation generated by a meter angle of vergence) decreases^{15,17} during incipient presbyopia. If the accommodation and vergence innervations needed for focusing and eye alignment, and the strengths of the cross-couplings between accommodation and vergence remain constant with age, then, within the linear portion of the accommodative stimulus-response curve, the response AC/A and CA/C ratios would not change with age.¹⁸ The empirically observed increase in response AC/A ratio^{15,16} and the decrease in response CA/C ratio^{15,17} with age both suggest that the neuromuscular effort expended to generate a given amount of accommodation (myodioter¹⁹) increases with age.¹⁷ The peak velocity of small accommodative step responses (1.00 to 3.00 diopters [D]) does not show a reduction with age despite large increases in lenticular viscosity,²⁰⁻²³ suggesting that there might be adaptive compensation to maintain youthful velocity of accommodation. If the neural control of accommodation is optimized for the biomechanical properties of the natural lens then, in principle, replacing the natural lens with accommodating IOLs that have different biomechanical properties would lead to mismatches between the neural control and biomechanics of the lens. The same effort used to control the older lens could be excessive for a more compliant prosthetic lens. What are the effects of such mismatches on the accommodative responses generated by accommodating IOLs, and what role does neural recalibration play in restoring optimal accommodative response characteristics?

The purpose of this article is two-fold. First, we conducted modeling simulations to explore the theoretical performance of two accommodating IOL prototypes when mismatches between the neural control and biomechanics of the lens are present. We also explored different aspects of neural recalibration that are relevant to the performance of prosthetic accommodating IOLs. Second, we present results from experiments on human adults that demonstrate the ability of neural control of accommodation to compensate for changes in effective biomechanics of the plant on a short-term basis.

MATERIALS AND METHODS

Pulse-Step Model of Accommodation

Detailed descriptions of the model and comparison with empirical data have been described previously for the accommodative step responses.^{24,25} Briefly, the pulse-step control engineering model predicts the dynamic properties of accommodative responses to step changes in optical defocus for different age groups (15 to 45 years). The model represents both the physical plant and the neural control system for accommodation. The biomechanics of the plant are characterized by viscoelastic coefficients and they are represented by springs (elastic element) and dashpots (viscous element) in the lumped model (Fig 1). The physical plant, organized after Beers and van der Heijde,² illustrates an opponent interaction between the lens capsule and choroid, which are connected via the lens zonules that pass through the ciliary body (see Fig 1A). The force applied by the choroid against the lens is modulated by the ciliary muscle (see Figs 1A and 1B). The effects of aging or of replacing the lens with an accommodating IOL can be simulated by entering its biomechanical properties into this lumped model.

The basic neural elements of the model, the phasic velocity and tonic position signals, are modeled after the phasic and tonic near response cells that drive accommodative and convergence responses,²⁶ and a pulsestep model of saccadic eye movements developed by Robinson²⁷ (Fig 2). The ballistic phasic velocity signal overcomes the viscosity of the plant and determines the dynamics of the accommodative step response. The feedback modulated tonic position signal overcomes stiffness of the plant to control the final size of the accommodative response (see Fig 2).²⁴ A combination of the phasic velocity and the tonic position signals innervate the ciliary muscle (see Fig 2).²⁴ The resultant ciliary muscle contraction force passes through the transfer function of the biomechanical plant (lumped model in Fig 1) to produce dynamic responses (see Fig 2). A web-based interactive version and Matlab/Simulink (The Mathworks Inc, Natick, Mass) downloadable versions of this dynamic model are available on our website (<http://schorlab.berkeley.edu> click on A-IOL model link).²²

The model can be used for two purposes. First, the biomechanical properties of the plant can be altered to predict how biomechanical changes, such as those occurring with aging or following implantation of an accommodating IOL, will influence the stability and speed of the accommodative response. Second, with reverse engineering, the necessary change in the activity of the phasic and tonic cells that would restore optimal response characteristics can be estimated.

Dynamic Performance of Accommodating Iols

The dynamic performance of two accommodating IOL prototypes was simulated using the pulsestep model in Matlab/Simulink. Because information about the effective biomechanical properties of current accommodating IOL designs is not readily available due to proprietary restrictions, we used estimates of their biomechanical properties that are suggested in the literature. Accommodating IOL I represents an injectable polymer that deforms to change power of the eye much like the natural lens.⁶⁻⁸ Accommodating IOL II represents an axially translating rigid lens that moves for and aft within the open fluid chamber of the lens bag and anterior chamber.⁹⁻¹¹ Accommodating IOL I was simulated by reducing both the stiffness and viscosity of the lens matrix to that of a natural 25-year-old lens therefore mimicking the reduced viscoelasticity of injectable polymers.^{6,7} Accommodating IOL II was simulated by reducing the lens matrix stiffness to that of a 25-year-old and doubling the lens viscosity from that of a 45-year-old therefore mimicking the reduced elasticity and the increased viscosity due to fluid drag.¹¹ All simulations used the neural control properties of a 45-year-old accommodative

system. These simulations are solely intended to demonstrate general trends in dynamic accommodation that could arise by modifying the lens biomechanics, and they do not represent the performance of any specific accommodating IOL.

Empirical Measures of Accommodation Adaptation

This study was aimed at providing a direct demonstration of the ability of the human adult accommodative system to undergo adaptive recalibration on a short-term basis. All individuals took part in the experiment after signing an informed consent form approved by the Committee for Protection of Human Subjects at the University of California, Berkeley. Adaptation was induced by double-step dioptric changes in defocus (300 trials over a span of 1.5 to 2 hours). In this paradigm, an initial step change in defocus is presented to initiate an accommodative response, and this is followed 350 ms later by a second step change in defocus that induces an unanticipated focus error in the accommodative response. This error is corrected by a change in the neuromuscular effort that is guided by feedback from focus errors. The double-step stimulus changes the relationship between the amount of defocus and the initial muscular effort needed to correct the focus error, just as if lens stiffness had been unexpectedly changed.²⁸ An increased muscular effort was required by a double-step that increased the defocus during the initial accommodative response (gain increasing adaptation) and a decreased muscular effort was required by a double-step that decreased the defocus during the initial accommodative response (gain decreasing adaptation). Repeated occurrence of the initial focus error might initiate an adaptive recalibration of the sensory-motor transform for defocus, which may be reflected in changes in the static and dynamic characteristics of single step-test responses as occurs in other oculomotor functions.^{29,30} Similar double-step experimental paradigms have been used to adapt saccadic²⁹ and vergence³⁰ eye movements to simulated muscle paresis.³¹

RESULTS

Dynamic Performance of Accommodating IOLs

Figure 3 shows the position and velocity profiles of accommodating IOL I (see Figs 3A and 3B) and accommodating IOL II (see Figs 3C and 3D) for a 2.00-D step change in accommodative demand. Both lenses generated a 2.00-D accommodative response with “lags” that are similar to adult empirical responses.³² However, the responses exhibit different dynamic characteristics (see Fig 3). The accommodative response generated by accommodating IOL I shows underdamped oscillations that are characteristic of the reduced stiffness and viscosity of the injectable polymer. Accommodative responses generated by accommodating IOL II were sluggish with an initial overshoot but no noticeable oscillations. The unstable oscillations are somewhat controlled in accommodating IOL II due to the higher effective viscosity of the lens (double that of a 45-year-old eye) (see Figs 3C and 3D).

Normal dynamics of accommodative responses could be restored by altering the strengths of the phasic velocity and tonic position neural signals (see Fig 3). For accommodating IOL I, normal dynamic responses were restored by decreasing the strength of both the phasic-velocity and tonic-position signals by approximately 72% and 76%, respectively. For accommodating IOL II, normal dynamic responses were restored by increasing the phasic-velocity signal and decreasing the tonic-position signals by approximately 58% and 72%, respectively.

Empirical Measures of Accommodation Adaptation

Results from a representative 18-year-old and 26-year-old individual who took part in the gain increasing and gain decreasing adaptation, respectively, are shown in Figure 4. The peak velocity of accommodation increases following gain increasing adaptation (see Fig 4B) and this increase was associated with a large overshoot in the accommodative response before it

attained stability (see Fig 4A). The peak velocity decreased with gain decreasing adaptation (see Fig 4D) and the post-adapt response was more sluggish than the pre-adapt response (see Fig 4C). In general, individuals adapted less to the gain decreasing paradigm that simulated decreases in lens stiffness than to the gain increasing paradigm that simulated increases in lens stiffness.

DISCUSSION

Overall, the modeling exercise illustrates that dynamic accommodative responses could be suboptimal when a mismatch is present between the neural control and biomechanics of accommodating IOL and optimal accommodative responses could be restored through neural recalibration. In general, changing the size of the phasic-velocity signal either increases or dampens the initial velocity of the response, and changing the size of the tonic-position signal enhances stability of the response.

The empirical study demonstrates that given enough training, both the younger and older individual could adapt to the optically simulated equivalents of increases and decreases in lens stiffness (see Fig 4). Changes in the accommodative response characteristics occurred within 1.5 to 2 hours (the duration of the entire experimental session), suggesting that this adaptive recalibration has a fairly rapid time course. The characteristics of adaptation and the neural mechanisms that subserve adaptive recalibration in our training paradigm are likely to be different from those encountered following surgical implantation of accommodating IOLs. For instance, our training paradigm does not address any form of adaptation that might occur in response to structural changes in the accommodative plant following accommodating IOL implantation. It therefore remains unknown whether the magnitude and rate at which adaptation occurred in our experiment can be directly extrapolated to those that might occur following accommodating IOL implantation. However, our results indicate that the accommodative system possesses the capacity to change its neural control and that this capacity might be used to compensate for any age- or environment-related changes in the plant biomechanics. The bias towards adapting to increased lens stiffness would be somewhat expected as the visual system is accustomed to adapting to age-related increases in viscosity, but not to reverse aging of the lens (such as those encountered with an accommodating IOL). Under natural conditions for development and aging, the lens always gets stiffer and more viscous so that there would be no need to evolve a response to decreases in these two biomechanical properties. Thus, there might be greater evolutionary pressure to adapt to normal age-related increases in viscoelastic properties of the lens.

Throughout life, the viscoelastic properties of the crystalline lens increase with age,^{22,23} and studies of dynamic accommodation indicate that the neuromuscular control of accommodation is able to adapt to these changes during the first four decades of life to maintain youthful accommodation dynamics.^{20,21,24} Overall, accommodation control of the older eye appears to be adjusted to shape a stiff and viscous lens. When this natural lens is replaced with a more compliant prosthetic lens, there is a potential mismatch in the neuromuscular control and the new plant could lead to instability of dynamic responses. If accommodating IOLs introduce large changes in effective lens viscoelasticity that cannot be compensated on a shortterm basis, then the ongoing efforts to develop surgical corrections for presbyopia (accommodating IOLs) may therefore encounter problems in matching the effective biomechanical properties of the prosthetic lens material and structure to the neuromuscular control properties of accommodation.

Our model simulations and demonstration of adaptation provide some insight into solutions to these potential problems. The simulations suggest that to maintain optimal dynamic accommodative responses with a compliant accommodating IOL, the effective viscosity of the

prosthetic lens might be kept high to avoid instability of dynamic accommodation. It is also possible that initial mismatches in neuromuscular control and effective biomechanical properties of the accommodating IOL could be reduced with neural adaptation. This adaptation appears to be naturally available to compensate for the normal age-related increases in viscoelasticity of the IOL. Even during gradual age-related changes in lens stiffness, adaptation is stimulated by mismatches between the amount of defocus and the muscular effort required to focus the retinal image. Our studies show that adaptation could also adjust to the reversal of aging properties produced by the accommodating IOL, but less effectively than to the natural increasing age-related changes.

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Figure 1.

A) Anatomical correlates for the Helmholtz-Gullstrand model of accommodation (adapted from Beers and van der Heijde²). **B)** Lumped biomechanical model of the different structures involved in accommodation (the accommodative plant).

Figure 2.
Signal processing sequence in the pulse-step model of accommodation. See text for details.

Figure 3. Model simulation of dynamic accommodative responses generated by two prototypical accommodating IOLs. **A, C)** Position profiles for accommodating IOLs I and II. **B, D)** Differentiated velocity profiles for accommodating IOLs I and II.

Figure 4. Representative empirical measures of **A, C)** accommodative position and **B, D)** differentiated velocity plotted as a function of time. Panels A and B show data obtained in the gain-increasing paradigm and panels C and D show data obtained in the gain-decreasing paradigm. Each position trace represents an average of five individual traces.