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Adaptation model of nearwork-induced transient myopia

George K. Hung[1]* and Kenneth J. Ciuffreda[2]

[1]Dept. of Biomedical Engineering, Rutgers University, 617 Bowser Road, Piscataway, NJ 08854-8014, USA and [2]Dept. of Vision Sciences, State College of Optometry, State University of New York, 100 E. 24th Street, New York, NY 10010, USA

Summary

A nearwork model was developed to determine whether variation in accommodative adaptation gain, K_A, can account for the differences in the dynamic decay timecourse following near work in hyperopes (HYP), emmetropes (EMM), early-onset myopes (EOM), and late-onset myopes (LOM). The model incorporated a proximal component into a previously-developed adaptation model of accommodation and vergence. It was used to simulate the nearwork-induced transient myopia (NITM) response following 10 min of congruent binocular near viewing (5 D, 5 MA). The accommodative adaptation gain, K_A, value was varied from 1.0 to 6.0 in increments of 0.5. For the hyperopes, an additional constraint was imposed wherein the accommodative response was biased on the under-accommodated side of the deadspace operator (i.e., depth-of-focus). In addition, the effect of prolonged nearwork was simulated by alternating between 1 hr of congruent near viewing (3 D, 3 MA) and 5 min of congruent far viewing (0.25 D, 0.25 MA) over a 160 hr period representing one work-month with 40 hours of nearwork per week. The steady-state rms value of the accommodative error was measured as a function of K_A. It was found that the NITM timecourses for HYP, EMM, EOM, and LOM could be simulated accurately using K_A values of 2.0, 2.5, 4.0 and 5.5, respectively. The long-term final steady-state rms of the accommodative error was found to increase from 0.182 D to 0.188 D as K_A increased from 1 to 6. This indicated a small and progressive increase in residual accommodative error for higher K_A values, which was associated with EOM and LOM. Thus, NITM for the different refractive groups could be quantified by the accommodative adaptation gain element, with K_A for the HYP, EMM, and EOM and LOM groups having lower, intermediate, and higher values, respectively. The larger rms for higher K_A values suggests that a myopic individual may have a predisposition to exhibit a slightly larger long-term accommodative error, which may stimulate axial elongation and in turn promote the progression of axial myopia. © 1999 The College of Optometrists. Published by Elsevier Science Ltd. All rights reserved

Introduction

Myopia is a clinical refractive condition that affects 25% of the adult population in the United States (Sperduto *et al.*, 1983) and at least 75% of the population in Asian countries such as Taiwan (Lin *et al.*, 1996). Myopia can be corrected by optical means, but the cost to the consumers in the United States for eye examinations and optical corrections is $4.6 billion per annum (Javitt and Chiang, 1994). Furthermore, the wearing of spectacles for myopia may restrict one's vocational options (Mahlman, 1982). Surgical techniques have been developed over the past 20 years to correct myopia (Javitt and Chiang, 1994), but they are expensive and may have side effects; moreover, they do not prevent the subsequent development of adult-onset myopia or other age-related refractive changes. Thus, myopia is a costly worldwide public health problem. For these reasons, the slowing of myopic progression, as well as the prevention of its initial occurrence, has been of considerable interest to clinicians and scientists alike. Yet, a deeper understanding of the underlying myopigenic mechanisms has only recently begun to evolve (Ong and Ciuffreda, 1995; Curtin, 1985;

*Corresponding author.

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Grosvenor and Flom, 1991; Rosenfield and Gilmartin, 1998).

The development of myopia has both genetic and environmental components (Goss and Wickham, 1995). Although genetic factors appear to play a larger role in early-onset myopia, modernday workstyles clearly suggest that environmental factors play a significant role in the later development of myopia (Ong and Ciuffreda, 1995). A particularly important environmental factor is that of prolonged nearwork, which has been especially implicated in the development of late-onset myopia (i.e., onset after age 15 years) (Ong and Ciuffreda, 1995).

Four refractive groups have been identified in terms of severity (and direction) of refractive error: hyperopia (HYP), emmetropia (EMM), early-onset myopia (EOM), and late-onset myopia (LOM) (Grosvenor and Flom, 1991). Quantitative measures would be helpful to differentiate between, and perhaps even predict, those who will develop myopia versus those who will not. Such a measure may be found by stimulating the accommodation system during near viewing, which produces lenticular-based pseudo-myopia, and then measuring the closed-loop temporal course of decay of the lens response back to the original far point of accommodation. This is referred to as the nearwork-induced transient myopia (NITM) paradigm (Lancaster and Williams, 1914; Ehrlich, 1987; Rosenfield *et al.*, 1992a; and Ong and Ciuffreda, 1995), with the difference between post- and pre-task values representing the NITM.

Previously, an adaptation model (Hung, 1992) was developed that quantified the effect of prolonged nearwork on the accommodative response. It successfully simulated experimental results on the dynamic accommodative behavior following prolonged nearwork, as well as during alternate nearwork and distance viewing (Henson and North, 1980; Sethi and North, 1987; Ciuffreda and Hung, 1992). In the present study, a proximal component (Hung *et al.*, 1996) was added to the adaptation model to provide a more realistic and comprehensive representation of the accommodation system and to extend the model to the NITM experimental results. An important parameter in the model, the adaptive gain, K_A, had been used previously to modify the time constant of the accommodative con-

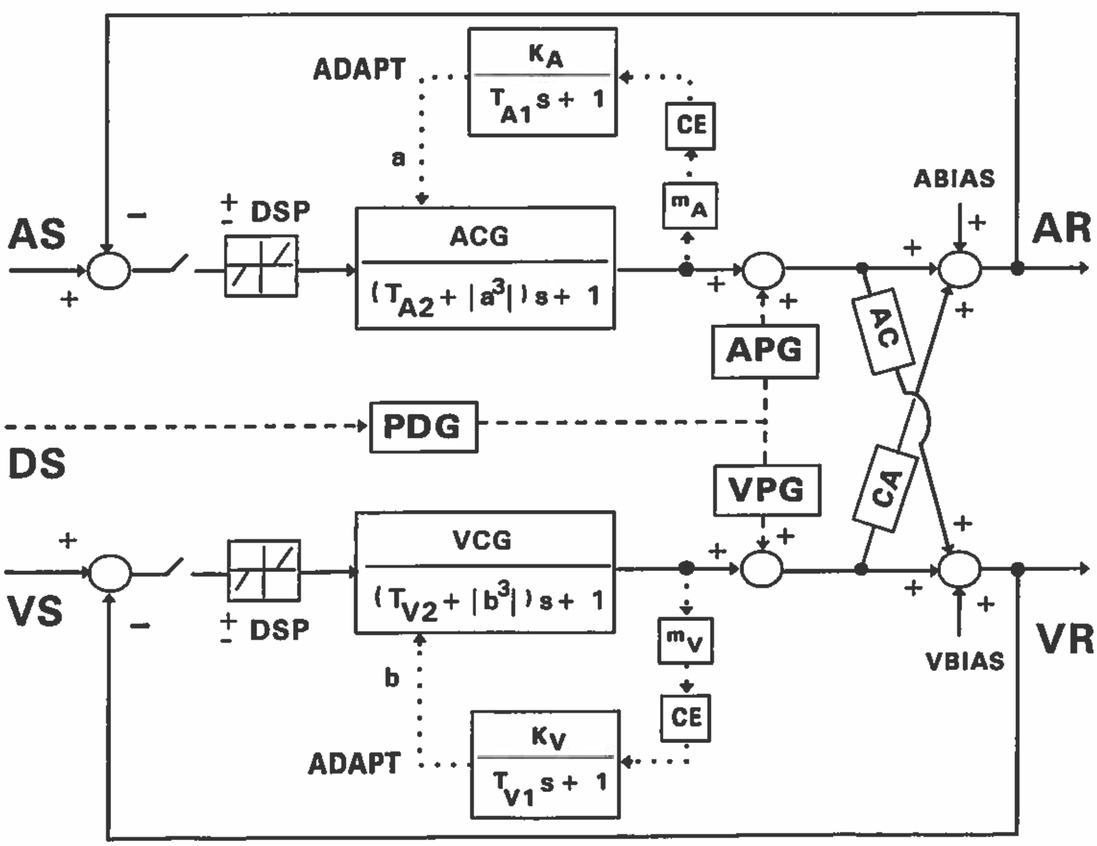

Figure 1. New nearwork oculomotor model. See text for details.

troller, and thereby control the rate of decay in the dark following an adaptation period. Simulations were therefore performed to determine whether variation in K_A could also account for the differences in the dynamic decay timecourse in the light following near work in the different refractive groups. In addition, the computer-simulated effect of higher K_A values on retinal defocus was examined over a 160 hr period, representing one work-month with 40 hours of nearwork per week, to assess its influence on the long-term development of myopia.

Methods

Modeling configuration

The nearwork model was based on a previously-developed static dual-interactive model of accommodation and vergence (Hung and Semmlow, 1980). It consisted of two feedback control loops driven by target defocus and binocular disparity, respectively (*Figure 1*). The two loops were connected via the accommodative convergence (AC) and convergence accommodation (CA) crosslinks. In the accommodative loop, the difference between the accommodative stimulus (AS) and response (AR), or accommodative error (AE) (i.e., retinal defocus), was input to the nonlinear deadspace element (DE), representing the depth-of-focus. If this input exceeded the depth-of-focus, then the output, which is now retinal image blur, was input to the accommodative controller having gain ACG. The accommodative controller output was summed with tonic accommodation (ABIAS) and the crosslink signal via convergence accommodation to provide the aggregate accommodative response. Also, the accommodative controller output was multiplied by the crosslink gain, AC, to provide the accommodative convergence signal. Similarly, in the vergence loop, the difference between the vergence stimulus (VS) and response (VR), or vergence error (VE) (i.e., retinal disparity), was input to the nonlinear deadspace element (DE), representing Panum's fusional area (Panum, 1858). If this input exceeded Panum's fusional area, then the output from DE was input to the vergence controller having gain VCG. The vergence controller output was summed with tonic vergence (VBIAS) and the crosslink signal via accommodative convergence to provide the aggregate vergence response. Also, the vergence controller output was multiplied by the crosslink gain, CA, to provide the convergence accommodation signal.

In addition to the basic dual-interactive model, the unique feature of this model was the incorporation of both adaptive (Hung, 1992) and proximal (Hung *et al.*, 1996) elements. The adaptive element in each loop received its input signal from the controller output, which in turn modified the time constant of the controller itself. For example, the accommodative controller output was input to a multiplier, m_A, and compression element, CE, to drive the adaptive element having gain, K_A, and time constant, T_{A1}. The multiplier and compression elements were necessary to provide a saturation effect for large inputs that was seen in the adaptation experiments (Fisher *et al.*, 1990; Rosenfield and Gilmartin, 1989). The adaptive element output, a, modified the time constant of the accommodative controller via the term, $T_{A2}+|a^3|$, where T_{A2} was the fixed portion of the time constant. The cubic relationship was obtained empirically to provide negligible increase in time constant for smaller amounts of adaptation, but a large increase in time constant for larger amounts of adaptation. Similar to the accommodative adaptation element, the vergence adaptive component consisted of multiplier, m_V, compression element, CE, adaptive gain, K_V, adaptive time constant, T_{V1}, adaptive element output, b, and controller time constant $T_{V2}+|b^3|$. It should be noted, moreover, that the relative contributions of the elements in the vergence loop to the aggregate accommodative response have been found to be very small (i.e., $<5\%$) under the closed-loop viewing conditions (Ong and Ciuffreda, 1997). Hence, these vergence parameters were not expected to play a significant role in NITM and the development of myopia. In contrast to the adaptive component, the input to the proximal component was represented by a distance stimulus (DS), which drove the perceived distance gain (PDG). The output of PDG was input to both the accommodative proximal gain (APG) and vergence proximal gain (VPG) elements, which were summed with the respective controller outputs (*Figure 1*). It has been shown that while the proximal component constituted a considerable percentage (up to about 80%) of the accommodative response under open-loop conditions, it provided a negligible contribution ($<4\%$) under normal closed-loop conditions (Hung *et al.*, 1996). Thus, under the closed-loop paradigms used in the present modeling study on NITM and long-term accommodative error, the proximal component is expected to play a very minor role. The proximal component is included in the model, however, for completeness of our new comprehensive nearwork model.

On the other hand, the accommodative adaptation gain plays a crucial role in inducing NITM due to its effect on the accommodative controller time constant. That is, after sustained nearwork, the increased accommodative adaptation element output would result in an increase in controller time constant. This in turn would result in a slower than normal return, or decay, of the NITM towards the pre-task baseline. Larger adaptive element gains produce slower decay rates, so that different gain values could be used to simulate NITM in the various refractive groups.

However, over the long-term, there are typically alternating periods of prolonged nearwork and brief distance viewing, which is representative of our everyday activities. Under this condition, both under-accommodation at near (lag of accommodation) and over-accommodation at far (lead of accommodation) typically occur (Ciuffreda, 1991, 1998; Ciuffreda and Wallis, in press). A useful measure of the long-term effect of the resultant retinal defocus on an individual, regardless of how it is generated, is that of the root-mean-square (rms) of the accommodative error. The rms error is essentially equal to the standard deviation about the mean value, so that a larger value is associated with greater retinal defocus. This measure was used in the prolonged near work simulation.

The parameter values were based on the adaptation and proximal models (Hung, 1992; Hung *et al.*, 1996). This included PDG = 0.212, APG = 2.1, ACG = 10.0, AC = 0.80 MA/D, ABIAS = 0.61 D, $m_A = 3$, $T_{A1} = 25$ sec, $T_{A2} = 4$ sec, and VPG = 0.067, VCG = 150.0, CA = 0.37 D/MA, VBIAS = 0.29 MA, $m_V = 0.5$, $T_{V1} = 50$ sec, $T_{V2} = 8$ sec, $K_V = 9$.

Model simulation

A computer program written in Quick-Basic was used to simulate the model in *Figure 1*. At the beginning of the program, a series of queries requested such parameters as the stimulus amplitude, timecourse, the feedback condition (i.e., open-loop in the dark and closed-loop in the light, etc.). A 4th-order Runge-Khutta integration routine was used to compute the outputs of the dynamic elements. The model response was graphed using a program written in MATLAB and displayed on a monitor. The graphs were plotted on a Laserjet4 plotter.

The nearwork model was used to simulate the NITM response (2 min at 0.17 D and 0.17 MA) following 10 min of congruent binocular near viewing at 20 cm (5 D and 5 MA). In the simulation runs, the K_A value was varied from 1.0 to 6.0 in increments of 0.5. The resultant NITM simulation curves were compared to and matched visually with the experimental results for the four refractive groups. For the simulation of the response of the HYP group, an additional constraint was imposed wherein the distance accommodative response was biased on the under-accommodated side of the deadspace operator (or depth-of-focus). This was done for consistency with the experimental results (Ciuffreda and Wallis, in press). In contrast, for the other three refractive groups, no such constraint was imposed so that the accommodative responses exhibited the normal slight (~0.25 D) over-accommodation for the far target (Rosenfield *et al.*, 1992b).

In addition, the effect of prolonged near work was simulated by alternating 1 hr of congruent nearwork (3 D, 3 MA) and 5 min of congruent far viewing (0.25 D, 0.25 MA) over a 160 hr period, which represents one work-month with 40 hours of nearwork per week. The final steady-state rms value of the overall (i.e., combined for distance and near conditions) accommodative error was measured and plotted as a function of K_A.

NITM experimental paradigm

The experimental paradigm used to obtain the NITM group data for the model simulations has been detailed elsewhere (Ciuffreda and Wallis, in press) and is described briefly below. After a 5 min period in total darkness to allow for dissipation of transient accommodative aftereffects (Ciuffreda, 1998), the pre-task refractive state of the right eye was assessed with the subject viewing binocularly 6/9 (20/30) Snellen letters, which were clearly seen by all subjects, at a distance of 6 m with moderate room illumination. A total of 20 readings were taken at 2 sec intervals, and the mean spherical equivalent, which represented the pre-task distance refractive state, was derived. Pre-task distance refractive variability (±1 s.d.) was generally no greater than ±0.1 D and was typically ±0.07 D in an individual subject. Following the pre-task assessment, a 10 min task was performed binocularly at near. The task consisted of viewing a target along the midline at 20 cm (5 D) which was comprised of a random matrix of black numbers on a white background (laser print). The angular subtense of each number was 7.5 min of arc (6/9, 20/30). Luminance was 40 cd/m^2, and contrast was 90%. Subjects were instructed to maintain the numbers in focus at all times. To ensure that clarity was maintained, the subjects were asked to perform simple mental arithmetic operations with the numbers during the entire task duration; in addition, this provided a moderate and constant cognitive demand. Furthermore, to assure accuracy, accommodation was measured periodically during the near task. Immediately after task completion (~2 sec delay), the subject's distance refractive state was reassessed, as described earlier for the pre-task condition. However, now 60 measurements were taken at approximately 2 sec intervals over the 120 sec post-task period. The post-task minus the pre-task difference represented the NITM. The data (mean spherical equivalent) for each subject were divided into 10 sec bin intervals and averaged.

Results

The model simulation NITM time courses for K_A values from 1.0 to 6.0 are shown in *Figure 2*. The NITM magnitude decayed to the baseline more slowly with increased K_A, with all curves reaching the pre-task level within the 120 sec time frame. The initial transient portion of the curves reflect both the large difference between the adapting (5 D) and the post-adapting (0.17 D) stimulus levels, as well as the differences in K_A values and their associated decay rates.

On the basis of these curves, K_A values corresponding to the experimental data of the four refractive groups were selected visually. It was found that the K_A values of 2.0, 2.5, 4.0 and 5.5 simulated reasonably accurately the experimental NITM time courses for HYP, EMM, EOM, and LOM, respectively. The experimental and corresponding model NITM time courses are plotted in *Figure 3a* and *3b*, respectively.

Because all viewing was done binocularly, a control experiment was simulated using sensitivity analysis (Hung and Ciuffreda, 1994) was performed to determine the effect of the vergence adaptation component via the vergence accommodation crosslink on NITM. Vergence adaptation gain, K_V, was varied from 5 to 20 in increments of 5, while maintaining all other parameters constant. It was found to have a negligible differential effect on the NITM curves (*Figure 4*).

Lastly, the final steady-state rms of the accommodative error after 160 hr of nearwork was plotted for different K_A values (*Figure 5*). There was a small but progressive increase in the rms of the accommodative error with increased K_A.

Discussion

Genetic factors may influence the link between K_A, defocus blur, and myopia development. These include both neuro-adaptive and biomechanical factors. For example, individuals may have a genetic predisposition to greater adaptive response during near viewing, resulting in transient over-accommodation at distance. This is seen as a slower accommodative decay of NITM that can eventually lead to an excess of cumulative, time-integrated retinal defocus, perhaps reflecting slightly impaired sympathetic activation (Strang *et al.*, 1994). Individuals may also have a greater susceptibility and biomechanical compliance of the ocular tunics to retinal defocus effects. Defocus effects on the retina may induce biochemical changes that result in an increase in axial length, which in turn lead to myopia (Goss and Wickham, 1995). The differential expression of these two genetic factors may be responsible in part for the variation of the degree of myopia found.

Environmental factors can act conjointly with an individual's genetic predisposition, serving as a trigger mechanism for the genetic component to become manifest, or perhaps they are simply additive. Thus, it may be possible for an individual to eschew nearwork, and the associated temporal increase in retinal defocus, to avoid or reduce the development of myopia, despite a familial genetic predisposition for myopia. Conversely, an individual may perform an over-abundance of nearwork, thus greatly increasing exposure to chronic retinal defocus, resulting in the development of

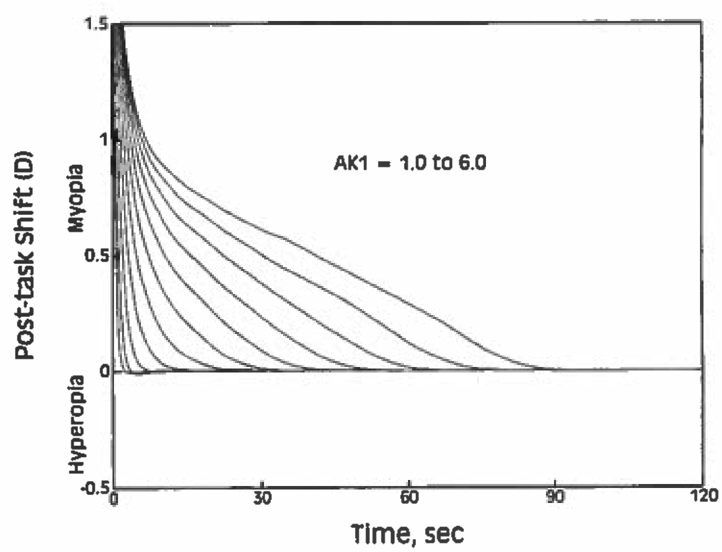

Figure 2. Model computer simulation of NITM as a function of accommodative adaptation gain value, K_A.

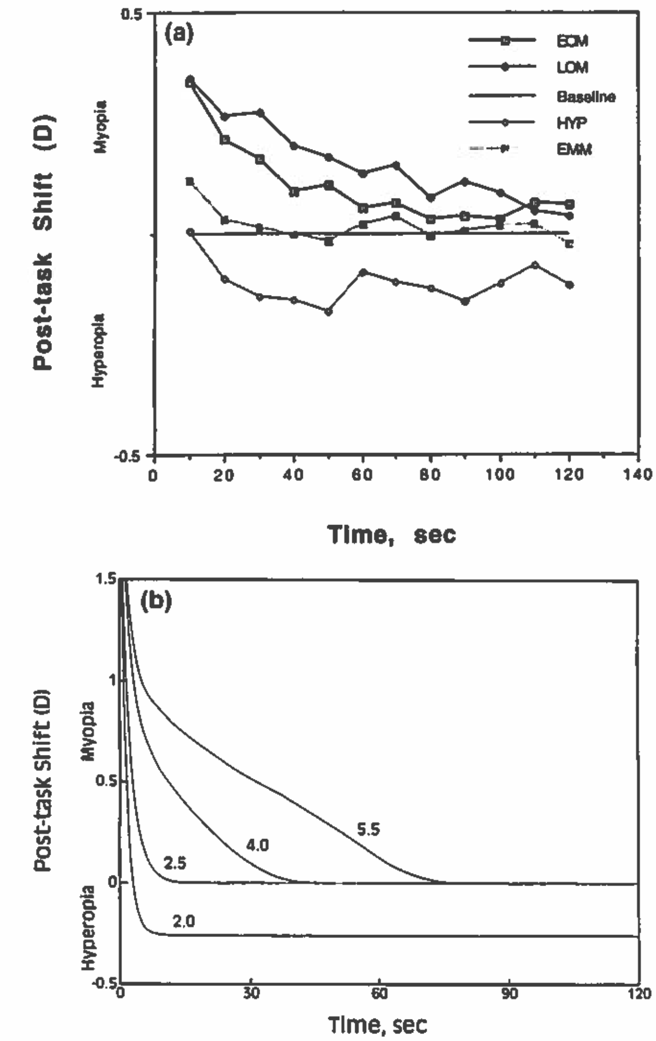

Figure 3. (a) Experimental results (pre-task baseline distance refraction variability was <±0.1 D) and (b) matching model computer simulation of NITM as a function of refractive group.

myopia despite the lack of such a familial genetic predisposition.

The emphasis of our present model-based study was the role of the adaptive component on the NITM time course. The adaptive element represented a neural-oculomotor feedback process that controlled the effect of sustained stimulation of the accommodative system during nearwork. The slowed decay of the distance accommodative response following prolonged nearwork was due to an increase in output from the adaptive element, thus resulting in an increase in the accommodative controller time constant. This decay was slower for larger K_A values. The long-term increase in exposure to accommodative error, and the resultant retinal defocus, was simulated using repeated

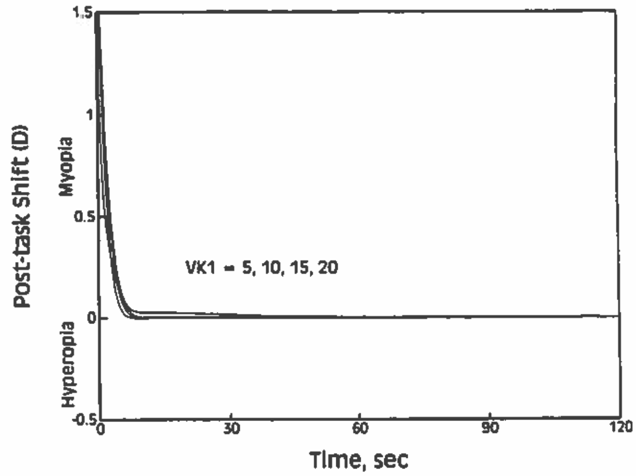

Figure 4. Model computer simulation showing effect of vergence adaptive gain, K_V, on NITM.

periods of prolonged nearwork and brief distance viewing, representing rest intervals. The resultant overall increase in retinal defocus, as reflected in the progressive increase in rms error, may be myopigenic in nature, where such defocus can induce increased axial length and in turn produce myopia (Ong and Ciuffreda, 1997; Jiang, 1997). Although the neuropharmacological and biomechanical susceptibility of the ocular tunics to retinal defocus was not modeled here, it is a significant portion of a current model-based study in our laboratory.

The NITM simulation results demonstrated that accommodative adaptation gain clearly discriminated the four refractive groups. The lower adaptive gain values (K_A = 2.0 and 2.5) corresponded to the HYP

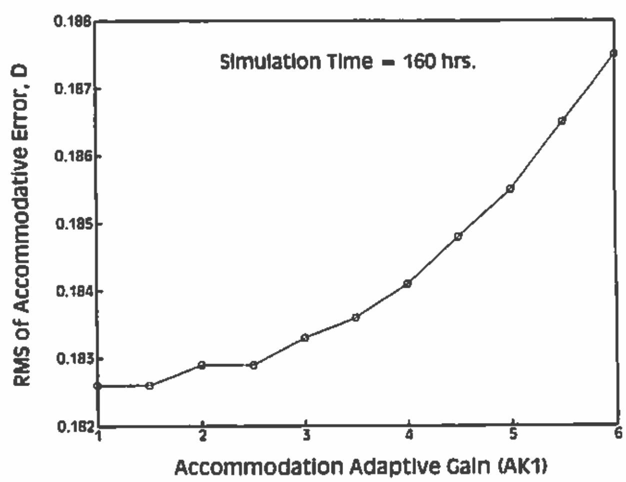

Figure 5. Model computer simulation showing effect of accommodative adaptation gain, K_A, on the rms value of accommodative error.

and EMM groups, respectively, whereas the higher adaptive gain values ($K_A = 4.0$ and 5.5) corresponded to the EOM and LOM groups, respectively. Thus, larger K_A values were associated with myopia, and perhaps may also be involved in pre-myopic development. This association could result from the small and progressive increase in the long-term rms of the accommodative error, and thus an increase in retinal defocus, with the larger K_A values.

Our nearwork model was able to simulate not only the adaptation (Hung, 1992) and proximal (Hung *et al.*, 1996) behavior in earlier studies, but now also the recent results on NITM time courses in different refractive groups. In the adaptation model (Hung, 1992) simulation, a 10% error criterion was used to determine the accuracy of fit to experimental data. Such versatility and robustness are important characteristics of an accurate and realistic model. In addition, its new quantitative measure of the rms of accommodative error provides insight into the potential role of adaptive gain on myopia development. Although the model appears to be relatively complex, it is parsimonious in that it uses a minimum number of parameters to represent the various response characteristics. For example, both refraction-based NITM and long-term rms of accommodative error are reflected in the variations in a single parameter, K_A.

Areas that need to be addressed in the future include: the interplay between retinal defocus, retinal biochemical and biomechanical factors, and the development of axial elongation; and, the relation between adaptive gain and the physical aspects of the eye. At present, the model results on NITM and long-term accommodative error are the first steps towards a more comprehensive and quantitative understanding of the underlying motor-based mechanisms in the development of myopia.

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