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AC/A ratios in myopic and emmetropic Hong Kong children and the effect of timolol

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Purpose: Caucasian children with myopia have elevated response accommodative vergence to accommodation (AC/A) ratios. The purpose of this study was twofold: to determine if response AC/A ratios vary with refractive error and with myopic progression rate in Hong Kong Chinese children, and to determine the effect of beta-adrenergic antagonism with topical timolol application on AC/A ratios.

Methods: Thirty children aged eight to 12 years participated in the study. All refractive errors were corrected with spectacle lenses. Accommodative responses were measured using a Shin-Nippon autorefractor and concurrent changes in vergence were assessed using a vertical prism and a Howell-Dwyer card at three metres and 0.33 metre. Accommodative demand was altered using plus or minus two dioptre lenses and lens- and distance-induced response AC/A ratios were calculated. Measurements were repeated 30 minutes after the instillation of topical timolol maleate (0.5 per cent).

Results: AC/A ratios appeared higher in progressing myopic children but the difference was not statistically significant. Timolol application reduced accommodative convergence (AC) in the stable myopes (reduction = -3 ± 1.14°) but not in the emmetropes (0.69 ± 0.96°) or progressing myopes (0.16 ± 0.43°) and this difference between refractive groups was statistically significant (F2, 27 = 3.766; P = 0.036). However, timolol did not produce a significant change in the accommodative response to positive or negative lenses or response AC/A ratios.

Conclusions: We did not find that AC/A ratios in myopic Chinese children were elevated and therefore, it is unlikely that elevated AC/A ratios are responsible for the high levels of myopia that occur in Hong Kong. The finding that timolol reduced AC in the stable myopes suggests that the autonomic control of accommodative convergence in these children may be different from that in emmetropic children and those with progressing myopia.

Key words: accommodation, convergence, ciliary muscle, myopia, sympathetic system

Prolonged nearwork appears to be associated with myopic development and accommodation may yet prove to be the link between nearwork and myopia. While there is no proven mechanism linking the two, one theory is that if accommodative accuracy during nearwork is not maintained, a defocused retinal image results, leading to myopic development (for reviews see Wildsoet and Goss). In considering whether variations in accommodation lead to development of myopia, there is considerable evidence demonstrating differences in accommodative responses between myopic and non-myopic individuals. For example, myopes demonstrate reduced accommodative responses, lower tonic accommodation and greater...
nearwork-induced accommodative adaptation compared with their non-myopic counterparts. It is unclear whether these abnormal accommodative responses promote myopic development or result from myopia.

The association between myopia and nearwork may also involve the vergence system. Authors of clinical studies have reported that the onset of myopia in children is associated with increased exophoria at near. Myopic children with near esophoria also demonstrate greater rates of myopic progression than those with orthophoria or exophoria. If convergence is involved in myopic development, the interaction between accommodation and vergence, that is, the AC/A ratio (the amount of accommodative convergence [AC] per unit of accommodative [A] response) becomes an important factor to consider. Caucasian children with myopia have elevated response AC/A ratios and it has been suggested that this elevated ratio is the result of reduced accommodative response at near or enhanced accommodative convergence. Gwiazda, Grice and Thorn proposed that AC/A ratios in myopes might reduce once the myopia stabilises, presumably due to an improved accommodative response or an exophoric shift in the near phoria. The latter has been observed by Goss, who found a tendency for near phoria to show an exphoric shift following the cessation of childhood myopic progression.

In light of the differences in accommodative response between refractive error groups, several investigators have proposed that an imbalance of the autonomic input to the ciliary muscle, particularly a sympathetic deficit, may give rise to anomalous accommodative responses that result in or exacerbate myopic development. It has been suggested that a sympathetic deficit results in increased susceptibility to nearwork-induced accommodative adaptation and an increased likelihood that retinal defocus associated with accommodative adaptation triggers the onset or progression of myopia.

Based on the dual innervation theory of accommodation, if a sympathetic agent is applied to increase the input from the sympathetic system, then the parasympathetic input should increase to maintain the net accommodative response, resulting in an increase in the AC/A ratio. Conversely, if a sympathetic agent is applied to decrease the sympathetic input, parasympathetic input should also decrease and this would decrease the AC/A ratio. Stephens showed that a non-selective adrenergic agonist (one per cent hydroxyamphetamine hydrobromide) produced a significant increase in AC/A ratio, whereas an adrenergic antagonist, produced a significant decrease in AC/A ratios. In a subsequent study, Rosenfield and Gilmartin found that timolol, a β-adrenergic antagonist, produced a significant decrease in AC/A ratio. In a subsequent study, Rosenfield and Gilmartin found that timolol reducing the sympathetic input to the ciliary muscle and that the lack of effect in myopic subjects was suggestive of an absent or reduced sympathetic input to the ciliary muscle.

The purpose of this study was to investigate accommodation and convergence functions of children in Hong Kong, where the prevalence of myopia, at 70 to 80 per cent, is one of the highest in the world. We hypothesised that if the reason for this high prevalence involves the accommodation/convergence system, the AC/A ratio would also be elevated in Chinese myopic children. In addition if, as suggested by Rosenfield and Gilmartin, there were reduced sympathetic input to the ciliary muscle in myopia, then timolol would have effects only in emmetropic children. Conversely, if the progression rate were the important factor, then timolol would reduce AC in stable myopes, in whom the sympathetic input to the ciliary muscle has presumably returned to normal but not in progressing myopic children.

METHODS

Our experiments involved measuring accommodation and heterophoria both before and after timolol application in emmetropic and myopic children. Response AC/A ratios for both conditions were then calculated.

Subjects

Thirty children aged eight to 12 years (mean ± SD = 10.6 ± 1 yr) were recruited from the Optometry Clinic at The Hong Kong Polytechnic University. The following steps were used to determine the subjective refraction:

1. non-cycloplegic autorefraction
2. subjective monocular refraction with blur-back (+0.50 D to blur the 6/9 line)
3. binocular balance (vertical dissociation)
4. final prescription.

All subjects had at least 6/6 visual acuity (corrected or uncorrected) in each eye on the Bailey-Lovie acuity chart and all of the subjects were free of ocular disease and oculomotor imbalance. No child had anisometropia or astigmatism greater than 1.5 D. The subjective refraction was used to correct refractive error during measurement and to classify the child into a refractive group.

Subjects were divided into three groups, based on the refraction results: emmetropes (spherical equivalent refractive error [SERE] [that is, spherical component + half of the cylindrical component] between -0.25 D and +0.50 D), stable myopes and progressing myopes (SERE of -0.75 D or greater). Information on myopia progression rate was obtained from past clinic records or the subject’s optometrist. Myopes were considered to be progressing if their SERE had increased by -0.50 D or more over the past two years.

The study was conducted in accordance with the requirements of both the Queensland University of Technology Human Research Ethics Committee and The Hong Kong Polytechnic University Human Subjects Ethics Sub-Committee. All children were given a full explanation of the experimental procedures and verbal agreement from the children and written consent from their parents. The experimental procedures were approved by the Ethics Sub-Committee of the Hong Kong Polytechnic University.

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informed consent of the parents was obtained before commencement of the study.

**Accommodation and vergence measurements**

Trial frames and lenses were used to correct the child’s refractive error, which was determined by subjective refraction. The frame was fitted with a pantoscopic tilt of 15 degrees to reduce reflections from the anterior surface of the lens to prevent interference with the operation of the autorefractor. Vergence measurements were taken using distant and near Howell-Dwyer cards, positioned at three metres and 0.33 metre, respectively. The sizes of the numbers on the distant and near cards were equivalent to 6/12 and N6, respectively. Children viewed the distant Howell-Dwyer card at three metres binocularly for five to 10 seconds and were instructed to keep the numbers on the card as clear as possible and to report if they started to become blurred. A minimum of five readings of accommodation in the right eye was then taken. With the child still looking at the target, a 6° base-down prism was placed in front of the right eye. The subject was asked whether two images were seen one above the other and to report if they started to become blurred. A minimum of five readings of accommodation in the right eye was then taken. With the child still looking at the target, a 6° base-down prism was placed in front of the right eye. The subject was asked whether two images were seen one above the other and to report if they started to become blurred. A minimum of five readings of accommodation in the right eye was then taken. With the child still looking at the target, a 6° base-down prism was placed in front of the right eye. The subject was asked whether two images were seen one above the other and to report if they started to become blurred. A minimum of five readings of accommodation in the right eye was then taken. With the child still looking at the target, a 6° base-down prism was placed in front of the right eye. The subject was asked whether two images were seen one above the other and to report if they started to become blurred.

**Drug treatments**

Proxymetacaine hydrochloride 0.5 per cent (Alcaine, Alcon) application was used to inhibit reflex lacrimation and increase corneal permeability and a period of five minutes was allowed before further drug treatments began. Testing was performed twice:

1. after binocular topical saline application
2. thirty minutes after binocular timolol maleate 0.5 per cent (Timoptol, Merck, Sharp & Dohme) application.

To standardise drug volumes, the preparations were instilled using a precision micropipette (20 µl of drug per eye). Eyelid closure and punctal occlusion were carried out for two minutes to minimise systemic absorption. To measure the ocular hypertensive effects of timolol, pre- and post-installation, intraocular pressures (IOP) were measured using a non-contact tonometer (CT-60, Topcon, Japan). Children with a history of current or past cardiac or respiratory conditions were excluded from participation.

To complete all testing at one visit, the drug trials were neither double-blind nor randomised. As the accommodation measurements were objective, this should have no bearing on the results obtained. As timolol maleate 0.5 per cent, a non-selective β-adrenergic antagonist, reduces IOP, it has been suggested that betaxolol (a selective β₁-adrenergic antagonist) may serve as a better control than saline to account for possible interaction effects between IOP and accommodative responses. To limit the number of medicated eye drops given to the children, we chose to use saline as the control agent. We found that timolol produced a significant reduction in IOP by an average of 3.0 ± 2.0 mmHg (t_{28} = 8.263, p < 0.001). The reductions of IOP found in emmetropes (3.9 ± 2.4 mmHg), stable myopes (2.6 ± 1.3 mmHg) and progressing myopes (2.6 ± 1.9 mmHg) were not significantly different (F_{2,27} = 1.293, p = 0.29).

**Data analysis**

Lentic effectivity was taken into account in all measurements. The ocular demand on accommodation (D) was calculated using the formula:

\[ \Delta \text{L}/(1 - d^*\text{Rx}) - 1 - d^*(L + \text{Rx}) \]

where \( L \) = accommodative stimulus (D) at the spectacle plane, \( d = \) vertex distance (m) and \( \text{Rx} = \) spectacle correction (D). Exophoria was scored as a negative number and esophoria as a positive number. Distance-induced AC/A was calculated using the formula:

\[ L_0/1 + d^*L_1 \]

where \( L_0 = \) spectacle accommodative response (D). Exophoria was scored as a negative number and esophoria as a positive number. Distance-induced AC/A was calculated using the formula:

\[ (\text{distance heterophoria} [\Delta] - \text{near heterophoria} [\Delta])/(\text{ocular accommodative response at distance} [D] - \text{ocular accommodative response at near} [D]) \]

Positive lens- and negative lens-induced AC/A ratios were calculated as:

\[ (\text{near heterophoria} [\Delta] - \text{near heterophoria} [\Delta] \text{with lens})/(\text{ocular accommodative response at near} [D] - \text{ocular accommodative response with lens} [D]) \]

Negative AC/A ratios or ratios greater than 20 were excluded as they were most likely to have been produced by noise in the measurements. On this basis, AC/A ratios from four emmetropes and three myopes (two progressing myopes and one stable myope) were excluded from the positive-lens induced AC/A data set and data from three emmetropes were excluded from the negative-lens induced AC/A data set. Unpaired Student t-tests were used to determine if differences in
heterophoria measurements, accommodative responses and AC/A ratios were present between emmetropes and myopes. One-way analysis of variance was used to assess differences between emmetropes, stable myopes and progressing myopes and Bonferroni post hoc comparison was used to compare each of the groups. Paired t-tests were used to compare saline and timolol trials. All data are presented as mean (± SD) unless otherwise indicated.

RESULTS

Ten emmetropes, five stable myopes and 15 progressing myopes were tested (Table 1). Young stable myopes were difficult to find in the Hong Kong population, as young myopes tend to progress.10,50 Emmetropes were younger than the stable and progressing myopes by an average of 2.3 and 1.6 years, respectively. The progressing myopes in this sample became myopic at an earlier age (by an average of 2.2 years) and exhibited a higher degree of myopia (by an average of 2.1 D) compared with their stable counterparts.

Accommodation

There was a small lead of accommodation while fixating at the distance target for emmetropes (0.22 ± 0.26 D) and myopes (0.19 ± 0.27 D) (t_{28} = 0.236, p = 0.815; Figure 1). At near, subjects tended to under-accommodate. The measured lag of accommodation to the 3.3 D stimulus was similar in emmetropic and myopic subjects (0.63 ± 0.31 D compared with 0.45 ± 0.37 D, t_{28} = 1.247, p = 0.222). Similarly, there were no statistically significant differences in the accommodative lag of emmetropes (0.65 ± 0.31 D), stable myopes (0.25 ± 0.62 D) and progressing myopes (0.50 ± 0.27 D) (F_{2,27} = 1.806, p = 0.183; Figure 1).

The additional +2 D lens almost eliminated the lag of accommodation (0.02 ± 0.47 D on average for all subjects), while the -2 D lens produced a greater lag of accommodation (1.11 ± 0.70 D compared with 0.50 ± 0.36 D with no additional lens). Accommodative responses to the +2 D lens were similar between emmetropes, stable myopes and progressing myopes (F_{2,27} = 0.584, p = 0.565; Figure 1). The -2 D lens stimulated a significantly greater lag of accommodation in the emmetropic subjects (1.64 ± 0.72 D) compared with the myopic subjects (0.92 ± 0.60 D) (t_{28} = 2.776, p = 0.01). The difference in the -2 D induced lag of accommodation of emmetropes (1.64 ± 0.72 D), stable myopes (1.18 ± 0.61 D) and progressing myopes (0.85 ± 0.60 D) was significant (F_{2,27} = 4.408, p = 0.022; Figure 1). Emmetropic subjects demonstrated a statistically significantly greater lag of accommodation compared with the progressing myopes (Bonferroni, p = 0.019).

Heterophoria measures

At distance, the majority of emmetropic children were close to orthophoria (-0.13 ± 0.95). While myopic children exhibited more exophoria (-0.76 ± 1.1), the difference was not statistically significant (t_{28} = 1.456, p = 0.156). At near, the mean heterophoria for myopes was -1.04 ± 1.95, which was not significantly different from that of the emmetropic subjects (-0.71 ± 2.41). In addition, there were no significant differences in near heterophoria between the emmetropes, stable myopes or progressing myopes (F_{2,27} = 0.068, p = 0.935; Figure 2).

All subjects became more exophoric with the +2 D lens (-2.63 ± 2.40 compared with -0.97 ± 2.03 with no lens). Near heterophoria with the +2 D was similar in emmetropes and myopes (t_{28} = 0.248, p = 0.748), however, there were no statistically significant differences in heterophoria position between the emmetropes and myopes (t_{28} = -0.324, p = 0.748), or between emmetropes, stable myopes and progressing myopes (F_{2,27} = 0.482, p = 0.622).

AC/A ratios

Myopes appeared to demonstrate higher AC/A ratios than emmetropes, for both lens-induced and distance-induced conditions (+ve lens: 3.24 ± 4.19/D compared with 2.46 ± 3.38/D; -ve lens: 2.69 ± 1.81/D).
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compared with $1.84 \pm 1.17^\Delta/D$; distance: $5.75 \pm 0.51^\Delta/D$ compared with $5.45 \pm 0.63^\Delta/D$). However the differences were not statistically significant (+ve lens: $t_{21} = -1.06$, $p = 0.301$; -ve lens: $t_{25} = -0.449$, $p = 0.657$; distance: $t_{28} = -1.288$, $p = 0.208$). There appeared to be a trend for higher lens- and distance-induced AC/A ratios in the progressing myopes but the differences between the groups did not reach significant levels (+ve lens: $F_{2,20} = 0.595$, $p = 0.561$; -ve lens: $F_{2,25} = 0.577$, $p = 0.569$; distance: $F_{2,27} = 1.416$, $p = 0.26$; Figure 3).

**Beta-antagonism**

Timolol did not produce statistically significant changes in AC/A ratios in the emmetropes or the myopes, for either the distance-induced ($t_{28} = -0.183$, $p = 0.856$) or lens-induced AC/A data (+ve lens: $t_{26} = 0.266$, $p = 0.793$; -ve lens: $t_{24} = 0.141$, $p = 0.889$). When myopia was classified as stable or progressing, there was still no effect (+ve lens: $F_{2,19} = 0.367$, $p = 0.701$; -ve lens: $F_{2,23} = 0.161$, $p = 0.852$; distance: $F_{2,27} = 0.05$, $p = 0.951$).

As the AC/A ratio is the ratio between accommodative convergence (numerator) and accommodation (denominator), analysis was also performed on the changes in AC and accommodation induced by timolol. Changes in AC due to timolol in the negative lens-induced AC/A data set were significantly different between emmetropes ($0.69 \pm 2.71^\Delta$), stable myopes ($-3 \pm 1.14^\Delta$) and progressing myopes ($0.16 \pm 1.84^\Delta$) ($F_{2,27} = 3.766$, $p = 0.036$). *Post hoc* analysis revealed that timolol induced a significantly more exophoric shift in AC in the stable myopes compared with the...
emmetropes (p = 0.048; Figure 4). The difference in the esophoric shift in the stable myopes compared with the progressing myopes was close to statistical significance (p = 0.058; Figure 4). Timolol did not produce any significant changes in accommodation in emmetropes, stable and progressing myopes (F(2,27) = 0.392, p = 0.679). Accommodation responses to the additional ± 2 D lenses following timolol instillation were not significantly different between the groups (+ve lens: F(2,27) = 0.901, p = 0.418; -ve lens: F(2,27) = 0.517, p = 0.602).

**DISCUSSION**

Response AC/A ratios in Hong Kong Chinese children were lower than those reported previously in Caucasian children and there was no statistically significant difference between refractive error groups. This does not support our hypothesis that elevated AC/A ratios are involved in the high prevalence of myopia in Hong Kong. While there were no statistically significant differences in near heterophoria, lag of accommodation or AC/A ratios between the emmetropic, stable and progressing myopic children, the results of the timolol trial suggest the possibility of differences between the sympathetic input to accommodation and convergence systems in stable and progressing myopes. This study provided only a cross-sectional view of the relationship between myopia and the oculomotor system and data were based on relatively small group sizes, particularly for stable myopes. These factors should be considered when assessing the outcome of our study. We discuss our data in terms of the roles of accommodation, convergence and the sympathetic input in myopia development.

**Esophoria, lags of accommodation and myopic progression**

Caucasian children who become myopic or myopes who progress faster have a more esophoric heterophoria position compared to emmetropic children. However, we did not find Hong Kong myopic children to be more esophoric at near than the emmetropic children. In addition, this sample of Hong Kong progressing myopic children was not more esophoric and they did not show a significantly greater lag of accommodation compared with the stable counterparts.

Traditionally, the tendency for myopic children to be esophoric at near is thought to occur secondary to excessive accommodative effort at near, which in turn induces excessive accommodative convergence. Alternatively, the increased esophoria may be associated with reduced accommodation and not excessive accommodation, as previous studies have found a significant correlation between reduced accommodative response and increased near esophoria. The hyperopic defocus resulting from the lag of accommodation in esophoric myopic children may be the trigger for further myopia progression and near additions, provided as bifocals or as progressive addition lenses, have been used to try to retard myopia progression. The association between lag of accommodation and esophoria may also be the reason for bifocal and progressive lenses appearing to be more effective in myopes with near esophoria, at least in Caucasian myopic children. In the randomised masked Hong Kong Progressive Lens Myopia Control Study, Edwards and colleagues did not find that progressive lenses were effective in retarding myopic progression in Hong Kong myopic children. However, this group included very few esophores. As we did not find Hong Kong myopic children to be more esophoric or to exhibit greater lags of accommodation compared with the emmetropic children, our finding might explain in part the lack of effect in the Hong Kong Progressive Lens Myopia Control Study.

**Elevated AC/A ratios and myopic progression**

The response AC/A ratios of the Hong Kong children were lower than those measured by Rosenfield and Gilmartin, Gwiazda, Grice and Thorn and Mutti and colleagues. Differences in the ratios may be due to differences in experimental technique and design. Rosenfield and Gilmartin and Gwiazda, Grice and Thorn used the Maddox rod, while we used the Howell-Dwyer card (modified Thorington method) for measuring heterophoric positions. Distance-induced AC/A ratios were on average higher than either of the lens-induced ratios. Gwiazda, Grice and Thorn also found higher AC/A for the distance-induced method and suggested that this may be explained by the proximity cues available.

We did not find response AC/A ratios, either distance- or lens-induced, to vary significantly with refractive error or myopic progression rate. This is contrary to studies that report elevated AC/A ratios in myopic subjects. Mutti and colleagues investigated the relationship between refractive error and AC/A ratio in children aged six and 15 years and concluded that an elevated response AC/A ratio was a risk factor for myopia onset, although only 15 of 727 children in the sample were incident myopes during the study period. Similarly, Jiang found elevated AC/A ratios in six of 31 emmetropic young adults who later became myopic. Our data do not support the notion that elevated AC/A ratios are associated with a higher myopic progression rate in Hong Kong Chinese children.

**Sympathetic input**

Timolol did not significantly alter accommodative responses or AC/A ratios, although timolol reduced AC in stable myopes but not in emmetropes or progressing myopes. This effect of timolol is consistent with the findings of Rosenfield and Gilmartin in a group of emmetropic young adults and demonstrates a sympathetic involvement during the near task. Rosenfield and Gilmartin proposed that the reduced AC was the result of reduced sympathetic input, which means a lower parasympathetic input is required to obtain the same net accommodative response. The reduced parasympathetic input was then reflected in the reduction in AC.

Our results support the hypothesis that timolol would have an effect on AC in stable myopes who presumably have an adequate sympathetic input to the ciliary muscle but have little effect on AC of progressing myopes with a sympathetic input.
CONCLUSION

While it cannot be concluded from our study that elevated response AC/A ratios are predictive of further myopic progression, longitudinal studies involving a larger sample and looking into differences in accommodative and convergence characteristics in Hong Kong myopic children are warranted. Studies investigating the autonomous control of accommodative and convergence systems in stable and progressing myopic children would also be useful.

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