

Training regimen involving cyclic induction of pupil constriction during far accommodation improves visual acuity in myopic children

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Purpose: Myopia in school-age children has become increasingly prevalent in industrialized countries, especially in Asia. A large population of school-age children still suffers from low visual acuity. We have developed a novel, safe and noninvasive training method to activate a pupillary constriction response during far accommodation that results in improved visual acuity.

Methods: Myopic children (n = 95) were treated for 3-minute sessions up to twice a week for 12–106 weeks. We stimulated quick cycles of near/far accommodation by displaying a visual object on a LCD screen and moving the screen in cycles from a near (25 cm) to a far (70 cm) point and back, while keeping the retinal projection size and brightness of the object constant.

Results: Mechanistically, we noted pupillary constriction upon far accommodation in trained myopic children, which was not seen in normal subjects or in untrained myopic children. Eighty five percent (52/61) of trained myopic right eyes with two sessions weekly experienced improved visual acuity (VA) by more than 0.1 logMAR units with an average improvement of 0.30 ± 0.03 standard error of mean (SEM) logMAR units. With maintained training, most eyes' improved VA stayed almost constant, for more than 50 weeks in the case of 12 long trained subjects.

Conclusions: This simple, short and safe accommodation training greatly improves the quality of vision in a large population suffering from refractive abnormalities.

Keywords: accommodation, visual acuity, myopia, pupil constriction, training regimen

Introduction

Myopia in school-age children has become highly prevalent in industrialized countries, especially in Asia, where it affects up to 50%–60% of school-age children.^{1–3} Myopia in children may progress because of refractive correction.⁴ Various therapies have been attempted to slow down the progression of myopia in school children. Progressive addition lenses showed either no,⁵ or only marginal benefits.^{4,6–8} Another therapeutic approach, to slow down the progression of myopia, has been the application of pharmacological agents such as the nonselective muscarinic antagonist atropine. Although this treatment has been somewhat successful in slowing myopic progression, clinical side effects remain to be resolved.^{9,10} Surgical interventions, such as keratectomy (laser in situ keratomileusis (LASIK) and photorefractive keratectomy (PRK)), are used to improve refraction. Although these interventions often treat adult myopia successfully, they are inappropriate for a small subset of myopic children and techniques not indicated for general myopia in growing children.^{11,12} A large population of school-age children still suffers from low visual acuity (VA).

Accommodation is the ability to change the focus of the eyes from distance to near (near accommodation) or near to distance (far accommodation);¹³ thus, accommodation allows the subject to maintain a sharp image of an object displayed at varying distances. Accommodation training improves VA following defocusing by inducing blur adaptation.^{14–16} Previous accommodation training has used standard objects of a fixed size, without compensating for changes in size and light intensity of their projected images onto the retina depending on the object-to-eye distance.¹⁷ Hence, when subjects adapt to a blurred image, they have also to adapt to changes in image size and light intensity, induced by the object at different distances from the eye. This may preclude the use of quick near/far accommodation cycles, as subjects complain of having difficulty and discomfort when trying to focus as the object moves towards and away from their eyes rapidly.

Here, we investigate a novel method of accommodation training as a treatment for enhancing VA in myopic children. In order to train our subjects with quick cycles of near/far accommodation, we designed an apparatus that keeps the retinal projection size and brightness of the visual object constant by displaying the object on a liquid crystal display (LCD) screen and adjusting its size and brightness while moving it, in fast cycles, from a near (25 cm) to a far (70 cm) point and back. This set-up allows the subjects (in either monocular or binocular vision) to comfortably maintain a sharply projected retinal image of the quickly moving object during fast cycles of near and far accommodation. The majority of our treated children experienced significant improvements in VA with as little as two training sessions of 3 minutes duration per week.

Materials and methods

A novel accommodation training device

We designed a novel accommodation training device that consists of a small (4") Thin Film Transistor (TFT)-LCD screen (Panasonic, Japan), which rests on a linear rail that allows it to be electronically moved forward and backward with the aid of a stepper motor (α step, AS55AA, Oriental Motor, Japan) (Figure 1A). This screen displays an object; in this study, a white circle on a black background (Figures 1A, 1B). A motion range of 45 cm was selected for this study from around minus 1.4 diopters at the far point (70 cm) to approximately minus 4 diopters at the near point (25 cm) of accommodation. The screen movements were controlled by a personal computer (Panasonic, Japan), allowing the operator to set the traveling speed of the forward and back movements

as well as the dwell time at each end. The backward and forward movement of the screen is illustrated in Figure 1C. During testing, the screen was held for 0.3 second in the near and far end positions, at 25 cm and 70 cm respectively. It was moved at a velocity of maximally 100 cm/sec into the far position and maximally 100 cm/sec into the near position to create a blurred image on the retina of a subject estimated from the reports of dynamic accommodation.^{18,19} The position of the screen is constantly measured and interfaced with the computer to allow the recording of the motion of the screen over time, and to control the LCD screen. Using the positional

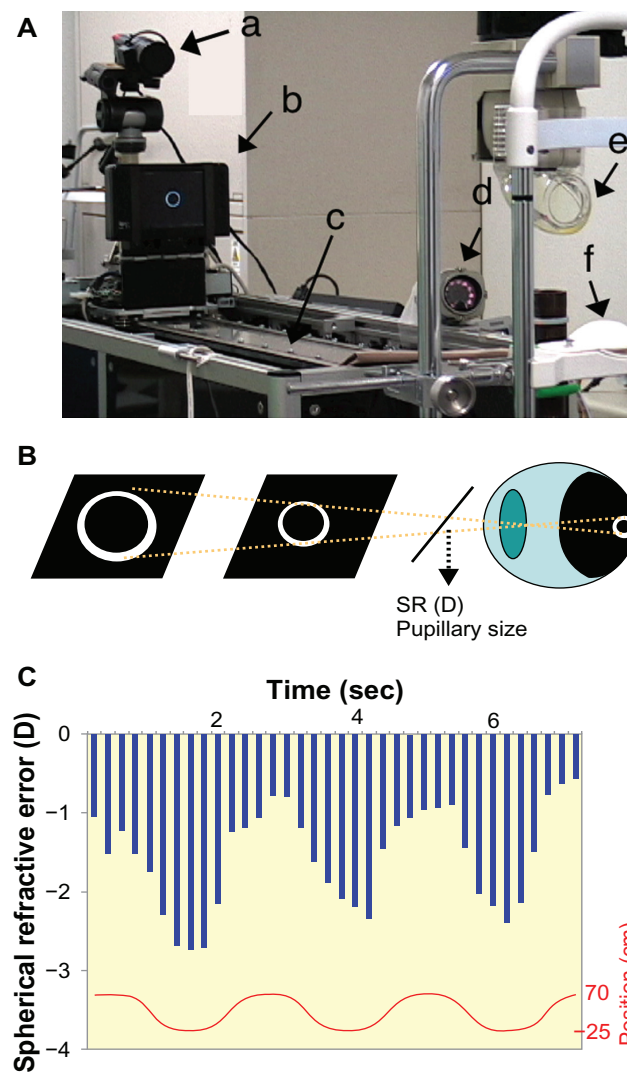


Figure 1A A photograph of the accommodation training device, which consists of an LCD screen on a rail. The arrows indicate (a) the infrared camera, (b) the LCD screen, (c) the rail, (d) the infrared ray, (e) the half mirror, and (f) the chinrest, respectively. **Figure 1B** This setup allows the researcher to project a visual object (here a ring) of apparent constant size and intensity onto the retina while moving the object forward and backward at a velocity of up to 1 m/sec. **Figure 1C** Three typical accommodation cycles of an emmetropic child are plotted in this illustration. The blue histograms represent the typical changes in refraction over time ranging from the far point (70 cm) to the near point (25 cm). The red line at the bottom shows the screen position over time. Note that the refraction changes follow the position of the screen.

data of the screen, the computer continuously adjusted the size of the circle in such a manner that its projection size onto the retina was kept constant.

At the 70 cm far point, the outer diameter of the circle used was 18 mm with 3 mm band width and at the near point 6.4 mm in diameter with a band width of 1 mm. The visual angle of this projection size to the retina was less than 1 degree to match the size of the fovea. The eye position of each subject was adjusted to the object vertically (by moving the chinrest position) and horizontally (by moving the position of the device). During the training sessions the brightness of the circle was kept constant, however, due to the decrease in circle area (fewer illuminated pixels on the screen) the amount of light traveling into the eye remained the same at any position (140 candela/m²). The contrast ratio of the TFT-LCD screen was 250:1. To simultaneously measure the refraction (spherical refraction, SR) of the eye, a half-mirror (dichroic mirror; cut-off wavelength for transmission: <680 nm, and the wavelength for reflection: <780 nm) was placed between the eye and the screen at a 45 degree angle which projected into a 'binocular open-field' refractor (FR5000S Grand Seiko, Japan).²⁰ The equipment could supply signals for the recording of refraction, an image of the pupil, or a positional signal on the LCD screen every 0.1 second. Refraction data were collected every 0.2 seconds. The positional data of the screen was used to align the changes in refraction (collected every other 0.2 seconds) with the cycle of the screen movement (Figure 1c). The images generated by the refractometer also allowed us to measure the size of the pupil (diameter in mm) every 0.2 seconds. The pupillary size of both eyes during training was usually monitored and recorded with an infrared camera (WAT902H3, WAT, Japan) equipped with a varifocal lens (YU10x5R4A-SA2, Fujinon, Japan). An observer could advise subjects to keep their gaze at the target when their attention drifted off the monitor screen.

Subjects

A total of 18 school-age children with myopia (subjective refraction (SR): ≤ -0.5 D) were recruited as a control group, in the setting of a private ophthalmology clinic. Progress of their VA (subjective refraction and uncorrected VA) and SR were measured twice: once at the beginning of the study; and once six or more months after the initial measurement. A total of 95 school-age children with myopia (SR: ≤ -0.5 D) were also initially recruited in the same setting and their spherical and cylindrical refractive errors were measured with a 'binocular open-field' autorefractor (FR5000S Grand Seiko, Japan). The diagnosis of myopia (SR: ≤ -0.5 D) was based on

a corrective eyeglass and all VA tests were performed by an independent assessor (orthoptist). They were not astigmatic (cylindrical refraction abnormality exceeding minus 1 D) and trained without corrective eyeglasses for 3 months or longer with 1–2 training sessions (each 3 minutes) weekly. Since the frequency of training was expected to influence VA improvement, these trained myopic children were separated into the following two different groups according to their frequency of training: children in group 1 were trained for 2 brief sessions per week, whereas those in group 2 received training once each week. Children in both groups were trained for at least 12 weeks, and had no additional visual abnormalities.

Visual acuity measurements

All measurements were performed once a week between 16:00–18:00 hours in order to minimize daily fluctuations of VA. For the measurement of VA at far distance (5 m), objects of decreasing size were displayed on a screen using a NIDEK TypeII SSC-300 chart. An examiner (an independent assessor) showed a Landolt ring using a remote control box to prevent any learning effects from subjects. The condition to pass each VA level required two correct answers in 3 examinations. The logMAR scale was used to allow for a comparison of our results with other studies.²¹ For the measurement of SR at far distance (3 m), a binocular open-field design FR-5000 (Grand Seiko, Japan) was used to minimize instrumental myopia. All results are given as mean \pm standard error of mean (SEM).

The effect of a pinhole (hole diameter: 2 mm, 3 mm, 4 mm, 5 mm) in front of the eye on VA was also examined. For this experiment, a pinhole ring plate was set in an eyeglasses frame and subjects kept their gaze on a Landolt ring through the hole. Cycloplegia was induced in one eye of 38 subjects by administering three drops of 1% cyclopentolate solution at 5 minute intervals to clarify whether spherical refractive errors measured by an open-field autorefractor were identical to cycloplegic autorefractive errors. All investigations and measurements performed in this study adhered to the tenets of the Declaration of Helsinki and were approved by the human experimentation committee of Kanagawa Dental College and Kikuna Yuda Eye Clinic. All subjects, and their parents, gave informed consent to take part after a full explanation of the nature and possible consequences of the study.

Results

We studied 187 school-age myopic children (age 6–12, of both genders). We found that spherical refractive errors (measured by an open-field autorefractor) and their uncorrected VA were

correlated with their SR (D) (Figure 2). The regression line of binocular open-field refractive errors was linear with 1.05 D/D of its slope, and was almost identical to the line of cycloplegic autorefractive errors.²² The gradient of the regression line, for the uncorrected VA, was 0.21 logMAR/D which was similar to data published by Laurance in 1926.²³

Frequent accommodation training leads to improved visual acuity

Myopia of affected school-age children is most often progressive.^{3,24} We confirmed that the uncorrected VA of untreated myopic children (control group) declined over time (Figure 3a; 18 healthy children/18 right eyes, aged 6–12, both genders). The rate of decline was 0.33 ± 0.05 logMAR/year, and was accompanied by progressive refractive disability (Figure 3b). Next, we aimed to improve VA of school-age myopic children using our novel accommodation training device. We tested for SR (D) of 95 healthy myopic children (183 eyes, aged 6–12, both genders), who trained on our accommodation device twice per week (3 minute sessions) for at least three months. Each session consisted of 30 seconds training of the left and the right eye separately, followed by 30 seconds training of both eyes after a 30 second rest. The individuals reported no discomfort while performing these near-far accommodations. VA was measured once per week before a treatment session as well as immediately after the treatment session throughout the entire treatment period. VA changes of Group 1 (2 training sessions per week) over the training period were calculated for each subject by regression

analysis and plotted as the VA before (blue dots) versus the VA after (red dots) the training period (Figure 3c). VA of the treated cohort improved significantly over the course of the study. Of the 61 eyes studied, 85% (52/61) of the VAs were improved from the level prior training by more than 0.10 logMAR units and 56% (34/61) by more than 0.20 logMAR units (the average improvement of the 61 eyes was 0.30 ± 0.03 SEM logMAR units, paired t-test $P < 0.001$), with 12 cases improving by 0.5 logMAR units. Raw data from two typical treated eyes (whose VA improved over time) are shown in Figure 4. While most eyes improved with training, two eyes had no change in VA after training, and two eyes showed a mild decline of VA (the average value of decline was 0.05 logMAR/year). The rate of decline of VA in these eyes is still less (better) than that found in average untrained myopic children (0.33 logMAR/year). Eyes of most Group 1 children (41 of 61) who trained on our accommodation device for longer than 12 weeks had improved VA at the 12 week point (eg, #83 Figure 4a). A small number of the children ($n = 11$) showed no training response in the first 12 weeks and then an improvement by a 30 week point (eg, #65, Figure 4c). With maintained training twice a week, most eyes' improved VA stayed almost constant, for more than 50 weeks in case of 12 long trained subjects (eg, #83, #65 Figures 4a, c). The average improved logMAR of the 57 left eyes and the total 118 eyes were 0.28 ± 0.03 SEM and 0.29 ± 0.02 SEM, respectively (paired t-test: $P < 0.001$).

The eyes of patients in Group 2 (trained on the accommodation device once per week) also showed enhanced VA following training, although this improvement was not substantial (Figure 3e). Of the 33 right eyes, 48% (16/33) of the eyes were improved by more than 0.10 logMAR units, and 27% (9/33) by more than 0.20 logMAR units. The average improvement of the 33 right eyes was 0.08 ± 0.03 SEM logMAR units (paired t-test, $P = 0.06$) and that of the left 32 eyes was 0.13 ± 0.03 SEM logMAR unit (paired t-test, $P < 0.05$). The average improved logMAR of the total 65 eyes (0.11 ± 0.02 SEM, paired t-test, $P < 0.001$) was less than half of the improvement experienced by eyes in Group 1.

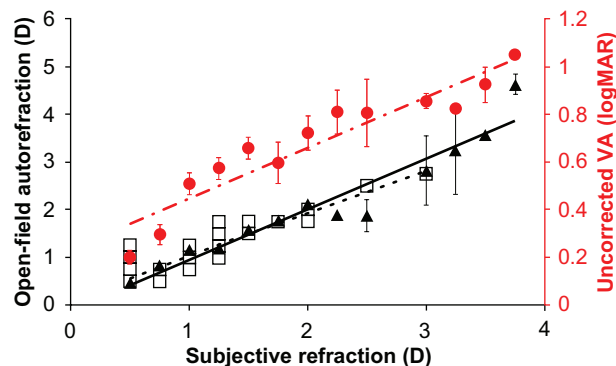


Figure 2 The relationship between uncorrected visual acuity (VA) and binocular open-field spherical refractive error (SR) with subjective refraction of 187 myopic school-age children. (●) and (---): Average values of uncorrected VA values in each 0.25 D interval from 0.5 D to 3.75 D and its regression line. Its slope was 0.21 logMAR/D. (▲) and (—): Average values in each 0.25 D interval from 0.5 D to 3.75 D of bifocal open-field refractive error and its regression line. Its slope was 1.05 D/D. (□) and (---): Cycloplegic autorefractive error and its regression line. Its slope was 0.89 D/D.

Potential mechanisms underlying training-induced enhancement of visual acuity

How did accommodation training stimulate improvement of VA in myopic children? VA is influenced by neural, retinal as well as optical properties of the eye, such as the lens and cornea and the length of the eyeball.¹³ We measured the SR

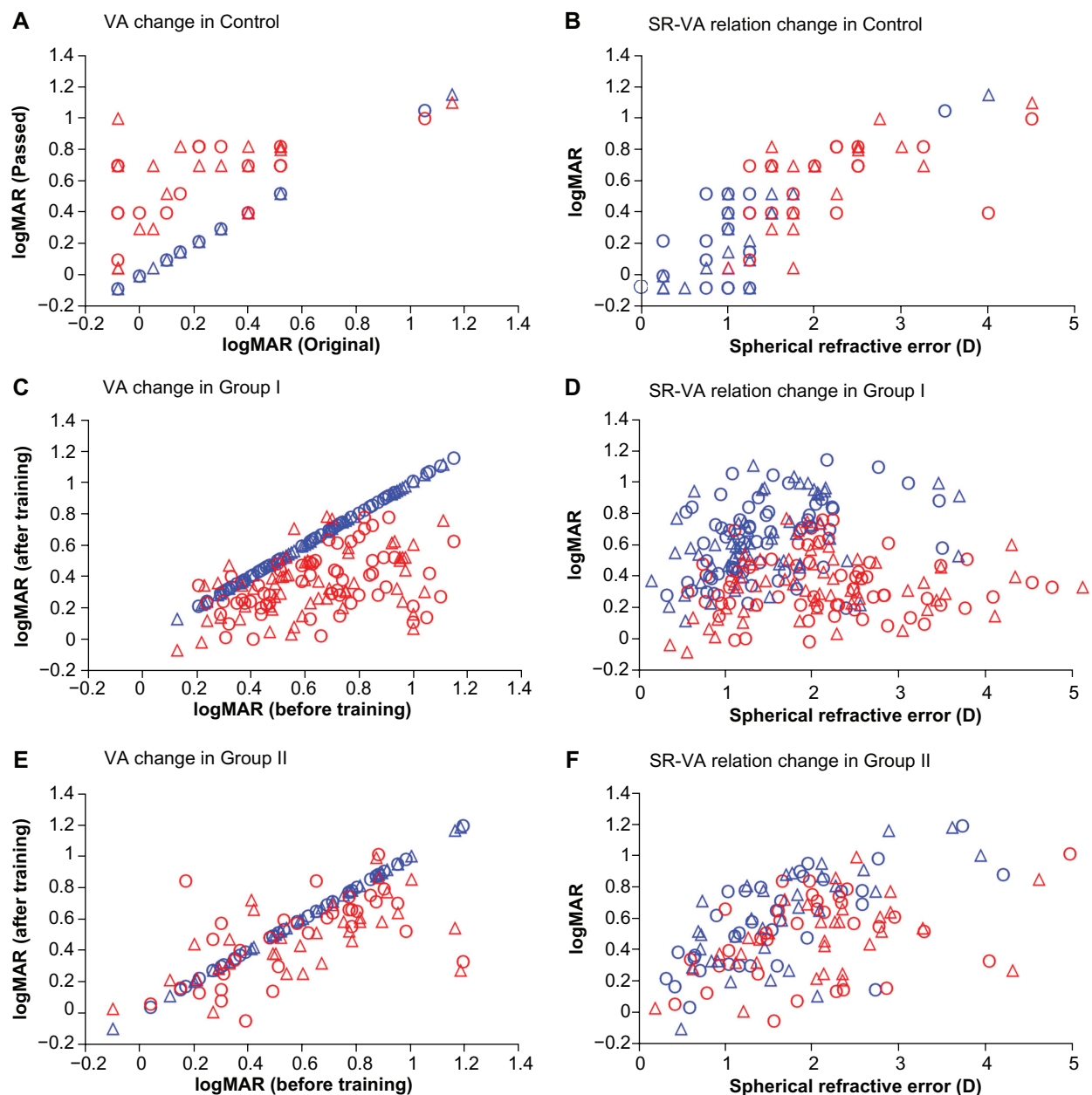


Figure 3 Accommodation training-induced improvements in visual acuity (VA) and spherical refractive error (SR) of eyes of school-age myopic children.

Notes: (blue plot; ○: right eye, △: left eye): at an original stage (a) or before training. (c,d), (red plot; ○: right eye, △: left eye): at a passed stage or after the training period of at least three months. In the left panels, the VA (in logMAR unit) at an original stage or before training is plotted using same value for both x-axis and y-axis (to generate a straight line; blue plot). **Figure 3A** and **3B** 18 control myopic school-age children that did not undergo training. **Figure 3A:** VA in untreated myopic children decreases (more positive) several months after initial measurement (paired t-test; $P < 0.001$ in right and left eyes). **Figure 3B** The relationship between VA and SR at initial measurement and after several months in untreated myopic children. There was a significant shift in the distribution of SRs in this group (factorial ANOVA; $P < 0.001$ in right and left eyes). **Figure 3C** and **3D** 61 myopic children (61 right eyes, 57 left eyes) in Group I (2 training sessions per week). **Figure 3C** VA of myopic eyes was improved (more negative) following frequent accommodation training for three or more months (paired t-test; $P < 0.001$ in right and left eyes). **Figure 3D** the relationship between VA and SR at initial measurement and after several months in eyes of frequently trained myopic children. There was a significant shift in the distribution of SRs in this group (factorial ANOVA; $P < 0.001$ in right and left eyes). **Figure 3E** and **3F** 34 myopic children (33 right eyes, 32 left eyes) in Group 2 (one training session per week). **Figure 3E** VA of myopic eyes was improved following training once per week for three or more months (paired t-test; $P = 0.06$ in right eyes, $P < 0.01$ in left eyes and all eyes). **Figure 3F** The relationship between VA and SR at initial measurement and after several months in eyes of myopic children trained once per week. Factorial ANOVA; $P < 0.05$ in left eyes and in total eyes, $P = 0.18$ in right eye.

of the eye at each training session. The SRs of Group 1 eyes declined by -0.018 ± 0.001 D per week (SEM, $n = 61$) over the duration of the training period (eg, Figures 4b, 4d). This change was similar to the decline observed in the Group 2

and in control myopic children (-0.021 ± 0.001 D per week). Thus, the improved VA in virtually all trained children was not due to improvements in the refractive error of the eye. In fact, VA was improved or maintained in trained eyes

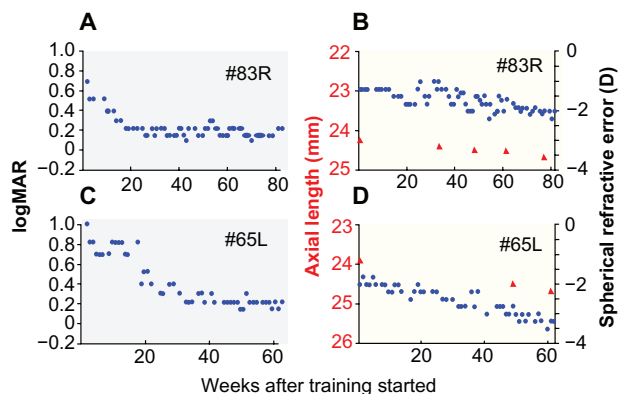


Figure 4 Examples of two common types of VA improvement (4a, 4c in logMAR units) and corresponding measurements of spherical refraction (SR) (4b, 4d, in diopters) over the time course of the training period from eyes of two myopic children.

Notes: VA and SR were measured weekly before each training session (blue circle ●). A regression line is calculated through all blue data points to quantify the changes in VA and SR from the beginning to the end of the training period. The individual in **Figure 4A** (#83) shows a marked early improvement of VA, despite a pronounced decline of the spherical refraction index **Figure 4B** shows the raw data from an individual that showed late improvement of VA. **Figure 4C** despite a pronounced decline of the spherical refraction index **Figure 4D** shows the raw data from an individual that showed improvement of VA. Red triangles (▲) indicate axial length in (4B) and (4D).

despite the further deterioration of the spherical refractive error (Figures 3d, 3f).

Another mechanism to improve VA is to decrease the size of the pupil. Therefore, we measured the diameter of the pupil during our near-far accommodation task (Figure 5). Children with normal vision, ie, emmetropia (EM, n = 12 right eyes), show a dilation of their pupils by 15% ($\pm 3.6\%$ SEM; from 4.6 ± 0.2 mm to 5.3 ± 0.1 mm SEM) when step accommodating from the near (30 cm) to the far (3 m) point of focus. A similar 12.4% ($\pm 2.0\%$ SEM; from 4.7 ± 0.1 mm to 5.2 ± 0.2 mm

SEM) increase in pupil diameter was also observed in untrained myopic children (UM, n = 23 right eyes). However, trained myopic children (TM) with improved VA demonstrated a constriction of their pupils of 5.6% ($\pm 1.7\%$; from 5.1 ± 0.2 mm to 4.8 ± 0.2 mm SEM) during far accommodation (n = 15 right eyes; Figure 5a). The trained group also demonstrated pupillary constriction from 3.9 mm to 3.5 mm diameter during binocular observation when they moved their target from a large Landolt ring (Snellen’s fraction 0.1) to a smaller one adjusted to their best VA (Figure 5b). A pinhole test showed that a 4 mm pinhole significantly improved VA and a further reduction of the pinhole to 3 mm was even more effective (Figure 5c).

The pupillary constriction was further corroborated by a phase shift of the pupillary diameter size relative to the changes in spherical refractive error during accommodation (Figure 6b). In other words, the pupillary diameter was minimal at the far point of accommodation. This result was confirmed by the video analysis of the pupils from trained 27 myopic children with improved VAs; all of them displayed pupillary constriction during far accommodation in the training.

Discussion

Here we described a novel, simple, non-invasive and safe method to enhance visual acuity in myopic children. We used a novel accommodation training device to introduce quick cycles of near/far accommodation by displaying a visual object and moving it in cycles from a near (25 cm) to a far (70 cm) point and back, while keeping the retinal projection

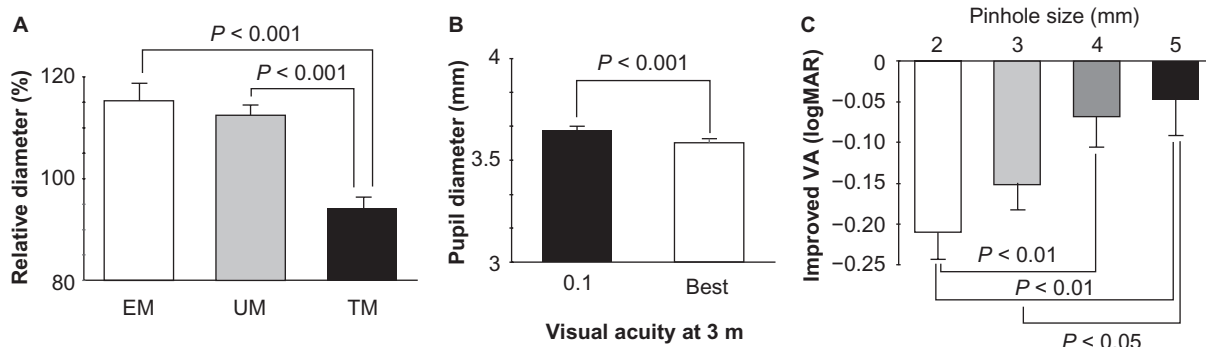


Figure 5 Training-induced pupillary constriction upon far accommodation.

Notes: **Figure 5A** This constriction was observed in trained myopic children (TM) (n = 15 right eyes) when step changing accommodation from 25 cm to 3 m. Emmetropic (EM) (n = 12 right eyes) and untrained myopic children (UM) (n = 23 right eyes) do not respond to step accommodation changes with a change in their pupil size. **Figure 5B** The pupil diameter of the trained group who correctly recognized a Landolt ring at their best VA (Best) had adjusted their VA to 3.50 ± 0.08 mm (n = 22 right eyes). Those recognizing a smaller Landolt ring at their best VA (Best) had adjusted their VA to 3.50 ± 0.08 mm (n = 44). **Figure 5C** The effects of four pinholes on VA were examined using diameters of 2 mm (2), 3 mm (3), 4 mm (4), and 5 mm (5), and were compared to the VA without pinhole (control (C)). The average improved VA (logMAR) value was -0.05 ± 0.04 (n = 18 right eyes) with a pinhole of 5 mm, -0.07 ± 0.04 (n = 18 right eyes) with a pinhole of 4 mm, -0.15 ± 0.03 (n = 18 right eyes) of 3 mm, -0.21 ± 0.04 (n = 18) of 2 mm respectively. All statistical analyses were performed by two-tail paired Student’s t test

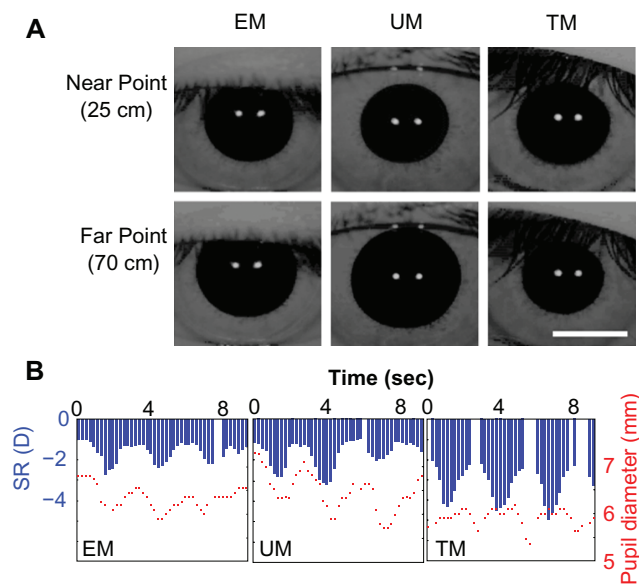


Figure 6 Pupillary size changing with accommodation. **Figure 6A** Both emmetropic children (EM) and untrained myopic children (UM) showed more than a 10% increase in pupil size during far accommodation (movement of the object from 25 cm to 70 cm). This reaction was reversed to a 12% decrease of pupil size in trained myopic children (TM). **Figure 6B** This pupillary constriction was further corroborated by a phase shift of the pupillary diameter size relative to the changes in refractive index during accommodation. This reverse reaction induced by the training was statistically confirmed between EM ($n = 30$ eyes) and TM ($n = 10$ eyes) and between TM and UM ($n = 8$ right eyes) (ANOVA, $P < 0.001$ and $P < 0.005$).

size and brightness of the object constant. By keeping the retinal projection size of our object constant we enabled our school-age children to follow the moving object at high speed without difficulty or discomfort. Our subjects showed pupil constriction during near accommodation before training onset, but at the end of the 12 weeks training period most children also constricted their pupils during far accommodation. This unusual pupillary regulation is probably the mechanism that underlies the improved VA, and this is supported by the training-induced pupillary constriction upon far accommodation shown in Figure 5.

Our method produced effective accommodation training in sessions of less than 3 minutes duration twice a week. The brevity of the training, and relative comfort experienced while training, encouraged many of our school-age myopic children to continue this regimen over a period of more than 3 months. The improved VA stayed almost constant with maintained training; in case of 12 long trained subjects for more than 50 weeks (eg, Figures 4A, 4C). Our preliminary study suggested that trained subjects with improved VAs could see a 20/20 object with less corrective glasses than those estimated by their refraction. This result suggests that the training may also improve the corrective level of eyeglasses. Since the training showed no adverse effect, we propose this method as a useful treatment for

school-age myopic children. We attribute these improvements in VA to the regular training sessions, because in children who stopped training, the beneficial effect was gradually attenuated and lost within a few months. This attenuation of improved VA following the conclusion of training on our device occurs sooner than it does after completion of training on NeuroVision (another device commonly used to correct vision)^{25,26} suggesting that our training mechanism may be different from NeuroVision. Several months after training had been completed, the VA of trained children was found to be comparable to that of untrained myopic children; however, the VA of trained children improved again once they resumed training (data not shown). Improvement in VA may be related to changes in the spherical refractive error, but our measurements of the SR at each training session revealed that the decline of this parameter (-0.018 D/w) was common to all three groups (group 1, group 2, and the control group), suggesting that it was independent of the training. This decline was similar to the values of progressive decline in SR reported in myopic children in Singapore (-0.88 D/year) and in Japan (-0.81 D/year).^{27,28} Declining VA and SR in myopia have been linked to excessive growth of the eyeball in a large number of cases. Our training did not prevent this excessive growth, as the increase in eyeball length was 0.010 mm/w in Group 1 and 0.012 mm/w in Group 2. The increase of other ocular dimensions were small, 0.058 mm/year in the anterior chamber depth and less than 0.01 D/year in the corneal curvature. Since the thickness of the lens scarcely changes during the growth period, increases in axial length may be the main component underlying the decline in SR.^{24,27} Hence, the improved VA in virtually all our children was not due to improvements in the SR of the eye. To the contrary, VA was improved and then maintained by continuing the training despite the further deterioration of spherical refractive error (Figures 3, 4). The continuous training may compensate a decreased VA level, caused by the decline of the refractive error, to keep the improved visual acuity level, because the decline of spherical refractive error increased the accommodative amplitude of the subject during training, that resulted in a retained, improved, VA level.¹⁴⁻¹⁶

Another mechanism to improve VA is to decrease the size of the pupil, which results in an increased depth of focus^{29,30} and a decreased spherical aberration.^{31,32} Pupil size regulation has been mainly studied in response to light stimulation but not in response to far accommodation; however, it has been shown during near accommodation in aged presbyopes.^{13,19,33} There has been no report on pupillary size regulation during far accommodation of school-age

myopic children. Pupillary constriction increases the depth of focus and decreases a spherical aberration, thus it is possible that pupillary constriction can improve a blurred image at a far site on the retina of myopic children as well as at a near site of a presbyopes. In fact, the pupil diameter of the trained children, with improved VAs, decreased in far accommodation at 3 m; and our pinhole test revealed that VA was also improved by wearing a 4 mm pinhole ring plate and further improved by a 3 mm pinhole. These results indicate that the observed pupil constriction from 3.9 mm to 3.5 mm in our children might indeed improve the VA by increasing depth of focus^{29,30} and reducing spherical aberration.^{31,32} This was confirmed by the pupillary constriction during far accommodation shown in our simultaneous measurements of pupil size and spherical refractive error (Figure 6b). This pupil constriction during far accommodation is a new finding. As pupil constriction is more effective on the VA improvement in small size pupils,^{29,30} our preliminary analysis suggested that the VA improvement of myopic children with small size pupils might be better than those with large size pupils.

What mechanism elicits miosis during far accommodation? Pupillary constriction is usually seen during near accommodation with convergence. But, myopic pupil size seems to increase steadily up to the age of about 20³³ and it appears that accommodative miosis below the age of 20 is reduced or absent.^{19,34,35} Furthermore, under some circumstances, accommodative miosis may be reduced or absent.^{36,37} These results suggest that near accommodation or convergence may not influence the pupil response of school-age myopic children to far accommodation. What elicits pupillary constriction during far accommodation in our training system? Our training system, similar to a Badal optical system,¹⁵ has the following specific characters: 1) the retinal image size is constant during accommodation, inducing only blur information to be available to drive the response;³⁸ and 2) a refractive error and pupil diameter continuously respond to the diopter change induced by the movement of the target. The target was accelerated from a near point (25 cm) to a point 30 cm from the eye to reach a maximal speed, 1 m/sec, and then moved at a constant speed 1 m/sec to a 65 cm point and finally it was slowed down from the 65 cm point to stop at the far point, 70 cm. During the movement from 30 cm to 65 cm the diopters of a subject to the target moving at a speed 1 m/sec changed with time according to a following equation; $D(t) = 1/(0.3 + 1xt)$ where t is time (sec). The changing rate of diopters dD/dt was shown as a following equation $dD/dt = 1/(0.3 + 1xt)^2$ indicating the speed was about

11.1 D/sec at a 30 cm point ($t = 0$) and 6.3 D/sec at a 40 cm point ($t = 0.1$ sec). Since the accommodation response-time from $-4D$ to $-2D$ of 0.76 sec in emmetropic children and 0.93 sec in myopic children, an average dD/dt was 2.5 D/sec in emmetropic children and 2.1 D/sec in myopic children.¹⁸ The average dD/dt (8.7 D/sec) from a 30 cm to a 40 cm was more than 3 times greater than the response speed, suggesting a blurred image may be elicited by the training. Under the cue-poor conditions of Badal stimulation, some individuals can exercise a greater degree of voluntary control over both accommodation³⁹⁻⁴¹ and pupil diameter.⁴² Figure 5b also indicates that a blurred image may induce pupillary constriction. These reports suggest that the blur stimulation by our system could elicit pupillary constriction during far accommodation. This hypothesis was supported by the training with a slow speed movement of the object (0.09 m/sec) which did not elicit pupillary constriction during far accommodation. The fact that monocular vision training elicited pupillary constriction as well as binocular vision training also confirms the hypothesis. Furthermore, it was harder to induce a pupillary constriction during far accommodation the training with a fixed object size indicating that the training with our device to keep a retinal image size of a object constant may be essential to elicit a pupillary constriction during far accommodation.⁴³

Subjects could not get a clear image from the object moving at a high speed indicating that the training in high speed may induce blur adaptation. Blur adaptation after distance fixation with various diopters improved unassisted VA of myopic observers by up to 0.27 logMAR without changing their pupil size.¹⁴⁻¹⁶ Blur adaptation induced by the use of our training device may also improve VA. Furthermore, since our dynamic training induced pupil constriction during far accommodation, the training may add such a pupil constriction effect to an improvement by the blur adaptation; which may enable some subjects to improve VA by over 0.5 logMAR. These high improvements were seen mainly in relatively severe myopic children ($<-2D$) (Figures 3C, 3D). It may be due to their accommodative amplitude in the training which was larger than that of children with less severe myopia. Since the brain and visual system are highly plastic, sizeable performance improvements have been documented in various aspects of vision after training.^{42,44-46} The repetitive training on our device might induce the gradual improvement of visual acuity and keep the improved VA level shown in Figure 4a and 4c through brain and visual plasticity. But the training could not slow down myopic progression. Since the mechanism to increase axial length has not been

clarified and there has been no useful therapy to slow down school age myopic progression, this problem remains to be resolved by future study.

Another possible mechanism to improve VA by this training is the learning effect. We reduced this effect while using the VA test instrument instead of a VA test sheet by indicating a symbol in the center of a screen which an examiner showed with a remote control box. This VA test was performed only once per week and was common in Group 1 and Group 2. However, as shown in Figure 3, increasing the training sessions from once per week (Group 2; Figure 3E) to twice per week (Group 1; Figure 3C) improved VA from 0.11 logMAR to 0.29 logMAR. These results indicated that the VA improvement may mainly be due to the training, and not the learning effect.

In conclusion, myopia in school-age children is progressive and their VA decreases 0.33 logMAR/year (Figure 3A), but our novel training method results in the significant improvement of VA in school-age subjects with myopia by blur adaptation and enhancement of iris function, and the improved VA remained almost constant with maintained training. This in turn controls pupil size, leading to increased depth of focus^{29,30} and decreased spherical aberration of the trained eye.^{31,32} The induction of pupillary constriction during far accommodation indicates that the training may also enhance blur adaptation to correct a blurred image, resulting in further improvement of VA. This simple, quick, comfortable and safe eye training will greatly improve the quality of vision in a large population suffering from refractory abnormalities. This development of a personal accommodation training device would allow many more myopic school-age children to enhance their VA and keep their improved VAs using a convenient method. Future work will address the efficacy of this method in improving the vision of adults with myopia, which has a prevalence 25% to 50% in the United States and Europe.^{47,48}

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References

1. Lin LL, Shih YF, Hsiao CK, Chen CJ. Prevalence of myopia in Taiwanese schoolchildren: 1983 to 2000. *Ann Acad Med Singapore*. 2004;33(1):27–33.
2. Matsumura H, Hirai H. Prevalence of myopia and refractive changes in students from 3 to 17 years of age. *Surv Ophthalmol*. 1999;44(Suppl 1): S109–S115.
3. Saw SM, Tong L, Chua WH, et al. Incidence and progression of myopia in Singaporean school children. *Invest Ophthalmol Vis Sci*. 2005;46(1):51–57.
4. Edwards MH, Li RW, Lam CS, Lew JK, Yu BS. The Hong Kong progressive lens myopia control study: study design and main findings. *Inves Ophthalmol Vis Sci*. 2002;43(9):2852–2858.
5. Grosvenor T, Perrigin DM, Perrigin J, Maslovitz B. Houston myopia control study: A randomized clinical trial. Part 2. Final report by the patient care team. *Am J Optom Physiol Opt*. 1987;64(7):482–498.
6. Fulk GW, Cyert LA. Can bifocals slow myopia progression? *J Am Optom Assoc*. 1996;67(12):749–754.
7. Gwiazda J, Hyman L, Hussein M, et al. A randomized clinical trial of progressive addition lenses versus single vision lenses on the progression of myopia in children. *Inves Ophthalmol Vis Sci*. 2003;44(4):1492–1500.
8. Kurtz D, Hyman L, Gwiazda JE, et al. Role of parental myopia in the progression of myopia and its interaction with treatment in COMET children. *Inves Ophthalmol Vis Sci*. 2007;48(2):562–570.
9. Chua WH, Balakrishnan V, Chan YH, Tong L, Ling Y, Ouah BL, Tan D. Atropine for the treatment of childhood myopia. *Ophthalmology*. 2006;113(12):2285–2291.
10. Ostrin LA, Frishman LJ, Glasser A. Effects of pirenzepine on pupil size and accommodation in rhesus monkeys. *Inves Ophthalmol Vis Sci*. 2004;45(10):3620–3628.
11. Carr J, Hersh P. Patient evaluation for refractive surgery. In: Azar DT, editor. *Refractive surgery*. Stanford, CT: Appleton and Lange; 1997. p. 101–109.
12. Paysse EA, Hamill MB, Hussein MA, Koch DD. Photorefractive keratectomy for pediatric anisometropia: safety and impact on refractive error, visual acuity, and stereopsis. *Am J Ophthalmol*. 2004;138(1): 70–78.
13. Glasser A, Kaufman PL. Accommodation and presbyopia. In: Kaufman PL, editor. *Adler's Physiology of the Eye*. St Louis, MO: Mosby; 2003: 197–233.
14. Cufflin MP, Hazel CA, Mallen EA. Static accommodative responses following adaptation to differential levels of blur. *Ophthalm Physiol Opt*. 2007;27(4):353–360.
15. Cufflin MP, Mankowska A, Mallen EA. Effect of Blur adaptation on blur sensitivity and discrimination in emmetropes and myopes. *Invest Ophthalmol Vis Sci*. 2007;48(6):2932–2939.
16. Rosenfield M, Hong SE, George S. Blur adaptation in myopes. *Optom Vis Sci*. 2004;81(9):657–662.
17. Tucker J, Charman WN. Reaction and response times for accommodation. *Am J Optom Physiol Opt*. 1979;56(8):490–503.
18. Culbane HM, Winn B. Dynamic accommodation and myopia. *Invest Ophthalmol Vis Sci*. 1999;40(9):1968–1974.
19. Kasthurirangan S, Glasser A. Age related changes in accommodative dynamics in humans. *Vision Res*. 2006;46(8–9):1507–1519.
20. Wolffsohn JS, Ukai K, Gilmartin B. Dynamic measurement of accommodation and pupil size using the portable Grand Seiko FR-5000 autorefractor. *Optom Vis Sci*. 2006;83(5):306–310.
21. Bailey IL, Lovie JE. New design principles for visual acuity letter charts. *Am J Optom Physiol Opt*. 1976;53(11):740–745.
22. Chat SW, Edwards MH. Clinical evaluation of the Shin-Nippon SRW-5000 autorefractor in children. *Ophthalmic Physiol Opt*. 2001;21(2):87–100.
23. Laurance L. *Visual Optics and Sight Testing*, 3 ed, London, UK: School of Optics; 1926.
24. Lam CS, Edwards M, Millodot M, Goh WS. A 2-year longitudinal study of myopia progression and optical component changes among Hong Kong schoolchildren. *Optom Vis Sci*. 1999;76(6):370–380.

25. Durrie D, McMinn PS. Computer-based primary visual cortex training for treatment of low myopia and early presbyopia. *Trans Am Ophthalmol Soc.* 2007;105:132–140.
26. Polat U, Sagi D. Spatial interactions in human vision: From near to far via experience-dependent cascades of connections. *Proc Natl Acad Sci U S A.* 1994;91(4):1206–1209.
27. Saw SM, Chua WH, Gazzard G, Koh D, Tan DT, Stone RA. Eye growth changes in myopic children in Singapore. *Br J Ophthalmol.* 2005;89(11):1489–1494.
28. Hasebe S, Ohtsuki H, Nonaka T, et al. Effect of progressive addition lenses on myopia progression in Japanese children: A prospective, randomized, double-masked, crossover trial. *Invest Ophthalmol Vis Sci.* 2008;49(7):2781–2789.
29. Campbell FW, Gubisch RW. Optical quality of the human eye. *J Physiol.* 1966;186(3):558–578.
30. Wang B, Ciuffreda KJ. Depth-of-focus of the human eye: theory and clinical implications. *Surv Ophthalmol.* 2006;51(1):75–85.
31. Oshika T, Tokunaga T, Samejima T, Miyata K, Kawana K, Kaji Y. Influence of pupil diameter on the relation between ocular higher-order aberration and contrast sensitivity after laser situ keratomileusis. *Invest Ophthalmol Vis Sci.* 2006;47(4):1334–1338.
32. Wang Y, Zhao K, Jin Y, Niu Y, Zuo T. Changes of higher order aberration with various pupil sizes in the myopic eye. *J Refract Surg.* 2003;19(2 Suppl):S270–S274.
33. MacLachlan C, Howland HC. Normal values and standard deviations for pupil diameter and interpupillary distance in subjects aged 1 month to 19 years. *Ophthalmic Physiol Opt.* 2002;22(3):175–182.
34. Schaeffel F, Wilhelm H, Zrenner E. Inter-individual variability in the dynamics of natural accommodation in humans: relation to age and refractive errors. *J Physiol.* 1993;461:301–320.
35. Gislén A, Gustafsson J, Kröger RH. The accommodative pupil responses of children and young adults at low and intermediate levels of ambient illumination. *Vision Res.* 2008;48(8):989–993.
36. Phillips NJ, Winn B, Gilmartin B. Absence of pupil response to blur-driven accommodation. *Vision Res.* 1992;32(9):1775–1779.
37. Stakenburg M. Accommodation without pupillary constriction. *Vis Res.* 1991;31(2):267–273.
38. Charman WN, Radhakrishnan H. Accommodation, pupil diameter and myopia. *Ophthalmic Physiol Opt.* 2009;29(1):72–79.
39. Marg E. An investigation of voluntary as distinguished from reflex accommodation. *Am J Optom Arch Am Acad Optom.* 1951;28(7):347–356.
40. McLin LN Jr, Schor CM. Voluntary effort as a stimulus to accommodation and vergence. *Invest Ophthalmol Vis Sci.* 1988;29(1):1739–1746.
41. Roscoe SN, Couchman DH. Improving visual performance through volitional focus control. *Hum Factors.* 1987;29(3):311–325.
42. Gislén A, Warrant EJ, Dacke M, Kröger RH. Visual training improves underwater vision in children. *Vision Res.* 2006;46(20):3443–3450.
43. Horie H, Hisahara S, Horie H, et al. To keep the object's retinal projection size constant is essential for induction of a pupillary constriction during far accommodation [Abstract]. Meeting of the Association for Research in Vision and Ophthalmology May 3–7, Fort Lauderdale, FL. 2009;S3923.
44. Fahle M, Poggio T. *Perceptual Learning.* Cambridge, MA: MIT Press; 2002.
45. Gilbert CD. Plasticity in visual perception and physiology. *Curr Opin Neurobiol.* 1996;6(2):269–274.
46. Li R, Polat U, Makous W, Bavelier D. Enhancing the contrast sensitivity function through action video game training. *Nat Neurosci.* 2009(5); 12:549–551.
47. Kempen JH, Mitchell P, Lee KE, et al. The prevalence of refractive errors among adults in the United States, Western Europe, and Australia. *Arch Ophthalmol.* 2004;122(4):495–505.
48. Vitale S, Ellwein L, Cotch MF, Ferris FL 3rd, Sperduto R. Prevalence of refractive error in the United States, 1999–2004. *Arch Ophthalmol.* 2008;126(8):1111–1119.

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