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Permalink

https://escholarship.org/uc/item/5f755668

Journal

Experimental Eye Research, 180(7)

ISSN

0014-4835

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Publication Date

2019-03-01

DOI

10.1016/j.exer.2018.12.010

Peer reviewed

The Effect of Part-time Wear of 2-Zone Concentric Bifocal Spectacle Lenses on Refractive Error Development & Eye Growth in Young Chicks

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Abstract

The purpose of this study is to characterize in young chicks the myopia control effects of part-time wear of two-zone concentric bifocal lenses. Nine-day-old chicks (n=115) were first made myopic with monocular −10 Diopter (D) single vision (SV) lenses worn for 3 days. Over the 6 days following myopia induction, either 1) two-zone bifocal lenses (−10 D center/ −5 D periphery, BFDC) were worn for 12 (full-time), 10, 8, or 6 h, with −10 D SV lenses worn for the remainder of the day, or 2) BFDC or BFNC (−5 D center/ −10 D periphery) lenses were worn every other day (EOD). Control birds wore −10 D SV lenses every day. Refractive error (RE) and axial ocular dimensions were monitored every three days with retinoscopy and high frequency A-scan ultrasonography respectively. Mean interocular RE and axial length differences after 3 days of myopia induction (± SEM) were −9.6 ± 0.19 D and 0.26 ± 0.01 mm across the groups. At the end of the following 6-day treatment period, equivalent values were: −10.66 ± 0.28 D, 0.42 ± 0.02 mm (SV-control); 1) −4.61 ± 0.29 D, 0.26 ± 0.02 mm (BFDC, 12 h); −4.82 ± 0.23 D, 0.28 ± 0.02 mm (BFDC, 10 h); −5.21 ± 0.27 D, 0.24 ± 0.02 mm (BFDC, 8 h); −6.34 ± 0.34 D, 0.25 ± 0.03 mm (BFDC, 6 h); 2) −8.29 ± 0.29 D, 0.32 ± 0.03 mm (BFDC, EOD), and −8.83 ± 0.36 D, 0.33 ± 0.03 mm (BFNC, EOD). Overall, full-time BFDC and part-time BFDC and BFNC lens groups exhibited similar changes and were less myopic than the SV group. The results suggest that bifocal lenses may have myopia control effects even when worn part-time, interleaved with standard (SV) myopic corrections, especially if worn for at least 6 h per day.

Keywords

Myopia; bifocal lenses; refractive error; axial Length; chicks

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Introduction

Myopia (near-sightedness) is an increasingly common condition that affects nearly one third of the population reported in one U.S. based study (Vitale et al., 2009). It is even more prevalent in East Asian countries, with some young adult populations recording startlingly high prevalence (e.g., 96.5%) (Jung et al., 2012). It was recently projected that ~50% of the world's population will be myopic by 2050, with 9.8% being highly myopic (Holden et al., 2016). Thus myopia raises significant public health concerns.

Traditionally, the management of myopia has been limited to optical devices and ophthalmic surgical procedures for correcting the focusing error, so restoring sharp distance vision. However, there is now increasing emphasis on controlling myopia progression in children, and to this end, contact lenses that either induce or incorporate multifocal optics (e.g., orthokeratology and soft multifocal soft contact lenses resp.), have been employed (Cho et al. 2005; Walline et al. 2009; (Aller and Wildsoet, 2008).

Although multifocal soft contact lenses have proven to be an effective treatment strategy for slowing myopia progression in children (Aller and Wildsoet, 2008; Li et al. 2017; Walline et al. 2011; Walline and Smith, 2015; Aller et al. 2016; Walline et al. 2017; Walline et al. 2013), it is not clear how important full-time wear (across the day) is to treatment efficacy. Single vision lenses may still be preferred for some visual tasks in the interest of optimal (clear) vision. The study reported here aimed to provide insight into the effects of interrupting such multifocal lens treatments on treatment efficacy, using the widely used chick model of ocular growth regulation.

Of relevance to the study described here, when optical defocus is imposed, such as, with single vision spectacle lenses, the eyes of young chicks have been shown to adjust their growth in compensation; specifically, the rate of axial elongation increases (decreases) with hyperopic (myopic) defocus imposed with negative (positive) lenses (Schaeffel et al. 1988; Howlett and McFadden, 2009; Hung et al. 1995). The inhibitory effect on eye growth of positive lenses (imposed myopia), has been found to be very enduring, persisting even when lens treatments are interrupted for short periods on a daily basis, while the growth enhancing effect of negative lenses (imposed hyperopia), quickly dissipates (NAPPER et al., 1997)Schmid and Wildsoet, 1996).

Paralleling the observation that multifocal contact lenses slow myopia progression in humans, concentric multifocal spectacle lenses that incorporate positive additions, have been shown to inhibit eye growth in previously untreated young animals, with appropriately designed lenses also inhibiting the effects of myopia-induced stimuli. Young chicks, guinea pigs, marmosets and rhesus monkeys have been subjects in relevant studies involving either 2-zone concentric lenses incorporating different powers in the center and periphery, or dual-power lens designs based on the Fresnel principle; in all cases, slowed eye growth and inhibition of the usual myopia-inducing effect of imposed hyperopia (negative power) were consistent observations (Liu and Wildsoet, 2012; (Liu and Wildsoet, 2011)McFadden et al. 2014; Arumugam et al. 2014; Arumugam et al. 2016; Tse et al. 2007; Benavente-Perez et al. 2012; Benavente-Pérez et al. 2014).

Based on the above results showing the enduring nature of responses to positive lenses, we hypothesized that the daily multifocal lens-wearing schedule could be reduced without significant reduction in their therapeutic benefit as a myopia control treatment. Building on results from our previous studies using two-zone (bifocal) spectacle lenses in young chicks, two studies were designed and completed, both again using young chicks as our model. In both cases, myopia was first induced with continuously worn single vision lenses, after which they were interleaved, either on a daily or alternate day basis, with two-zone lenses designed as myopia control treatments. In the study involving alternate-day wear, both concentric distance or near center lens designs were tested.

METHODS

Animals

White-Leghorn chicks, hatched from fertilized eggs obtained from University of California, Davis, were used in this study. They were reared in a normal diurnal white lighting environment (12 h on/12 h off), with food and water freely available. A total of 115 birds were used in this study, organized into 7 treatment groups. All animal care and treatments in this study conformed to the ARVO Statement for the Use by the Animal Care and Use committee of the University of California, Berkeley.

Treatments

Nine-day old chicks were fitted with monocular −10 D single vision (SV) lenses for 3 days to initiate myopia progression, after which chicks were randomly assigned to one of seven treatments. With the exception of one of two control groups that continued to wear the −10 SV lenses over the following 6 days, all other groups were exposed, at least part of the time over this 6-day period, to two-zone bifocal (BF) lenses combining −10 and −5 diopter (D) powers, either as a distance center design (BFDC; −10 D center/ −5 D periphery) or near center design (BFNC; −5 D center/ −10 D periphery). One of the latter groups wore the BFDC lens full-time over the following 6 days, as an additional control. For three BF groups of chicks, the −10 D SV lens was replaced with a BFDC lens for a block of time each day, either 10, 8, or 6 h in duration, initiated at 11:30 am, 1:30 pm, and 3:30 pm each day, respectively. BFDC lenses were replaced with −10 D SV lenses every day at 9:30 am ("lights-on") for each group. For two other groups, a −10 D SV lens was alternated every other day with either a BFDC or BFNC lens respectively. The lenses were switched immediately after the lights turn on, at 9:30 am. In all cases, fellow eyes were left uncovered as controls. Table 1 summarizes the treatments and group sizes.

All lenses had an overall diameter of 12.2 mm, an overall optical zone diameter of 10 mm, and in the case of two-zone lenses, a central zone diameter (CZD) of 4.5 mm. The effective add for both BFDC and BFNC lens designs was 5 D. These parameters were based on lens designs used in two of our previous studies, the results from which provided the frame work for the studies described here (Liu and Wildsoet, 2012; Liu and Wildsoet, 2011). Due to eye movements, only limited regions of the central and peripheral retina had consistent defocus experiences, while the paracentral region was alternatively exposed to the defocus arising from the central and peripheral lens zones. Based on a vertex distance of 3.3 mm, the

corresponding unifocal central visual field is estimated to be 12° in diameter, and widths of the unifocal peripheral and multifocal paracentral fields, 13° and 35° respectively. (Liu and Wildsoet, 2011). The lenses were mounted on velcro rings, with matching rings of loop Velcro affixed to the feathers surrounding one of the chick's eyes using collodion glue by way of attaching the lenses to the chicks. Lenses were cleaned and inspected at least 4 times daily to ensure that the lenses had not decentered, i.e., their optical centers were approximately aligned with the pupil centers of the chicks' eyes.

Measurements

Baseline refractive errors and ocular dimensions were measured before the start of lens treatments, using static retinoscopy and high-frequency A-scan ultrasonography, respectively, with follow-up measurements taken at the end of the initial 3-day treatment period (with −10 D SV lenses), and at 3 days intervals thereafter (Fig. 1). Refractive error measurements were made on-axis (centrally), as well as 30° nasally and temporally. For A-scan ultrasonography measurements, at least 7 traces were captured per eye and analyzed off-line. All measurements were made between 3:00 and 5:30 pm under gaseous anesthesia (1.5% isoflurane in oxygen), using eyelid retractors to hold the eyes of the chicks open during the measurements.

Data Analysis

Data analysis made use of Prism 6 (GraphPad Software, La Jolla, CA, USA). Spherical equivalent refractive errors (RE; average of results for the two principal meridians) were derived for use in data analysis. Optical axial lengths were derived as the sum of the axial dimensions of the first three ocular compartments (anterior chamber, lens and vitreous chamber). Derived interocular differences (treated eye – fellow control eye), are reported as mean ± SEM for each group. To analysze differences in treatment effects, two-way repeated measures ANOVAs were applied in combination with a Bonferroni post hoc test to longitudinal refractive error and ocular dimensional data. Select data are also shown graphically, normalized to day 3 values (baseline for BF lens treatments), with additional graphical analyses included as a supplement.

RESULTS

Effect of SV lens wear

All 7 groups were subject to the same initial −10 D SV lens treatment over three days when, as expected, their treated eyes elongated faster than fellow eyes, as reflected in the increases in vitreous chamber depths (VCDs) and thus optical axial lengths (ALs). Over this period, the choroids also thinned, contributing to the observed AL changes and, as expected, treated eyes showed myopic shifts in their refractive errors (REs). The mean interocular differences in RE and AL at the end of the 3-day treatment period, for all 7 groups combined, reflect these changes, i.e., −9.6 ± 0.19 D and 0.26 ± 0.01 mm. The change in refractive error represents almost full compensation for the imposed defocus at this time.

Effect of continuous wear of 2-zone lenses (BFDC) compared to SV lenses wear

For the control group that continued to wear the −10 D SV lens, their refractive errors remained relatively stable over the following 6 days thereafter, although their eyes continued to show accelerated elongation, presumably reflecting the developmental decrease in ocular refracting power (cornea and lens). In contrast, the control group wearing BF lenses full-time showed regression of their induced myopia, which is reflected in a reduction in VCD and thus AL (Table 2, Figure 2). The mean interocular differences in RE and AL at the end of the 9-day treatment period for the latter group are −4.61 ± 0.29 D and 0.26 ± 0.02 mm compared to −10.66 ± 0.28 D and 0.42 ± 0.02 mm for the −10 D SV control group (Table 2).

The AL data for treated and fellow (contralateral control) eyes of the −10 D SV and BF control groups are plotted separately (normalized to day 3) in Figures 3A and 3B, to examine the origin of the above difference, i.e., to directly assess the effect of wearing a BF lens on the elongation of treated eyes. For the −10 D SV group, the ALs of treated eyes grew faster than their fellows, as reflected in the divergence over the treatment period of the lines representing treated and fellow eyes. In contrast, the treated and fellow eyes of the BF group showed more similar rates of elongation, as reflected in the parallel alignment of the respective lines. These different ocular growth patterns are reflected in the statistically significant differences in the treated eyes of the −10 D SV and the BF groups on days 6 and 9 (P< 0.0001, P<0.0001, respectively). On the other hand, no statistically significant difference was found between the fellow eyes of these groups on either day 6 or day 9.

Choroidal thickness changes contributed to the axial length changes, with choroidal thinning over the intial 3 days of the −10 D SV lens wear. For the control group that continued to wear −10 D SV lenses, choroidal thinning also prevailed through out the entire treatment period. In contrast, for the BF lens group, this early thinning response had largely disappeared by day 6, although choroidal thinning was again apparent by day 9. Interocular differences in choroidal thickness at the end of the treatment period were −0.024 ± 0.01 mm for the −10 D SV control group and −0.047 ± 0.02 mm for the BF group. This paradoxical, statistically significant difference between the two groups, i.e., greater thinning in the BF group (P= 0.006), likely reflects, at least in part, the greater initial choroidal thinning recorded by this group at the end of the initial 3-day myopia induction period (P=0.005) (Table 3).

Effect of daily, part-time wear of 2-zone BFDC lenses on myopia progression

While full-time wear of 2-zone BF lenses allowed significant, albiet partial recovery from the initially induced myopia, as expected, part-time daily wear was also beneficial . Indeed, with respect to interocular differences in AL, there was no statistically significant differences between any of the 3 groups given more limited daily exposure to BF lenses, compared to the control group wearing the BF lenses full-time. In the case of interocular differences in RE, only the group with the shortest, 6 h exposure to BF lenses proved to be significantly different from the group wearing BF lenses full-time (12 h) (P= 0.0002) (Table 2, Figure 2). In other words, a strong inhibitory effect of the BF lenses on ocular elongation was retained, even with a reduction in daily exposure by up to 50%. Compared to the interocular difference in RE of −4.61 ± 0.29 D for the full-time BFDC lens group, values for

the groups with reduced exposure to the same lens design are significantly different in only one case, i.e., −4.82 ± 0.23 D (10 h, NS), −5.21 ± 0.27 D (8 h, P= 0.578), and −6.34 ± 0.34 D (6 h, P= 0.001). Equivalent interocular differences in AL are 0.26 ± 0.02 mm (full-time), 0.28 ± 0.02 mm (10 h, NS), 0.24 ± 0.02 mm (8 h, P= 0.619) and 0.25 ± 0.03 mm (6 h, NS). Changes in VCD over the treatment period closley mirror the AL changes for all groups (Figure 2).

For both treated and fellow (control) eyes, there are no statistically significant intergroup differences in the changes over the 6 day BF treatment period, i.e., for the 10, 8, and 6 h BFDC exposure groups compared to the changes in the full-time exposure group, when normalized to day 3 values (Treated eyes: P=0.102, 10 h; P= 0.926, 8 h; P= 0.678, 6 h; fellow eyes: P= 0.229, 10 h; P= 0.362, 8 h; P= 0.258, 6 h (Figure 4).

The patterns of change over the treatment period in interocular differences in choroidal thickness for the three groups wearing BFDC lenses part-time are also not significantly different from that of the group wearing BFDC lenses full-time. At the end of the treatment period, interocular differences in choroidal thickness were −0.025 ± 0.012 mm (P= 0.704), −0.011 ± 0.012 mm (P= 0.239), 0.003 ± 0.02 mm (P= 0.365) for the 10, 8, and 6 h groups, respectively (compared to −0.047 ± 0.02 mm for BF control group; Table 3).

Effect of every other day 2-zone BFDC and BFNC lens wear on myopia progression

When alternated every other day with −10 D SV lenses, both BFDC and BFNC lenses tended to normalize ocular elongation, just as seen with full-time (daily) wear of the BFDC lens, and there was no difference in the myopia control effects of BFDC versus BFNC lenses. These trends are evident in the graphical plots of normalized interocular differences in REs, ALs and VCDs across the 6-day treatment period (Figure 5), which are also summarized in Table 2.

While the group that wore BFDC lenses full-time exhibited the least myopia (−4.61 ± 0.29 D), the groups that wore either a BFDC or a BFNC lens interleaved with a −10 D SV lens every other day also have significantly reduced interocular differences in REs (−8.29 ± 0.29 D; P<0.0001 and −8.83 ± 0.36 D; P<0.0001, respectively), relative to that of the group wearing −10 D SV lenses full-time (−10.66 ± 0.28 D)(Table 2).

Interocular differences in AL for the part-time BFDC and BFNC lens groups (0.32 ± 0.03 & 0.33 ± 0.03 mm resp.) are similar to that of the group wearing BFDC lens full-time (0.26 ± 0.02 mm) and not significantly different (BFDC, P=0.24; BFNC, P=0.07). In contrast, the interocular difference in AL for the full-time −10D SV group (0.42 ± 0.02 mm) is significantly larger than those of three BF groups (P<0.0001) (Table 2).

The growth patterns of treated and fellow eyes over the 6-day BF lens treatment period were also individually analyzed for the two part-time BF lens-wearing groups. From Figures 6A and 6B, it can be seen that for these two groups, treated and fellow eyes exhibit approximately matching growth patterns. There is also no statistically significant difference between the changes in treated and fellow eyes when normalized to day 3, for either of the part-time BF lens groups (BFDC, P= 0.098; BFNC, P= 0.168 respectively).

The choroidal thickness changes in the groups wearing BFDC and BFNC lenses part-time are also similar in pattern to that of full-time BFDC lens group, although there are subtle differences. Interocular differences at the end of the 9-day treatment period are −0.041 ± 0.014 mm (NS) and 0.01 ± 0.01 mm (P= 0.025) for the part-time BFDC and BFNC groups respectively. That the group wearing BFNC lenses part-time exhibited apparently less choroidal thinning at the end of the treatment period may reflect the central location of the add, resulting in a larger area of central retina experiencing myopic defocus. Note that in both groups, the early thinning detected on day 3 had largely disappeared by day 6, these measurements following a day of BF lens wear. Measurements on day 9 followed a day of SV lens wear, which may partly account for the re-emergence of choroidal thinning in one of these two groups.

Lens-induced off-axis refractive error changes

No statistically significant differences were found between central (on-axis), nasal, and temporal REs at any measurement point, for any of the 7 treatment groups, when nasal and temporal RE were each compared with central RE for each group on days 3, 6, and 9.

Discussion

To our knowledge, this is the first study to address the effect of reduced (part-time) wear of myopia controlling BF lenses on progression. Our current study made use of 2-zone concentric bifocal lens designs, which were intended to simulate the effect created by concentric bifocal contact lenses used to control human myopia progression. To this end, our chicks first wore −10 D SV lenses for 3 days to initiate myopia progression before the introduction of the BF myopia control treatments. Our BF lenses had negative powers in both zones, the higher power serving to induce further myopia or correct it, while the lower negative power zone provided a positive add, located in either the center or periphery of the lens, depending on the design.

As expected, BFDC lenses worn for 12 h were effective at slowing myopia progression compared to SV lenses, which was reflected in reduced ocular elongation, as evident in the changes in VCD and axial length. To our surprise, wearing BF lenses for as little as 6 h per day was as effective as full-time BF lenses wear in controlling further myopia progression. We also found exposure to either BFDC or BFNC lenses every other day to be beneficial at slowing myopia progression, which was apparent in the VCD and AL patterns. Nevertheless, this treatment regimen was not as effective as full-time BF lens wear.

In earlier studies in chicks, the effect of interrupting single vision lens wear by short periods of normal vision was found to vary significantly, depending on the sign of the lenses worn. Hyperopia was consistently observed in response to positive lenses, although the size of the response was reduced when lens-wearing time was reduced. In contrast, the development of induced myopia was prevented when negative lens wear interrupted with as little as 3 h of normal vision (NAPPER et al., 1997; Park et al., 2003; Schmid and Wildsoet, 1996). The effect of imposed myopic defocus also tends to dominate with periodic exposure to myopic and hyperopic defocus across the day. For example, it was shown that brief periods (e.g., as little as 8 min) of myopic defocus imposed by positive lenses, can prevent the myopia

inducing effects of negative lenses worn for the reminder of the day in chicks (Park et al., 2003; Winawer et al., 2005; Zhu et al., 2003). Results from another study involving tree shrews, more closely related to the current one, also demonstrated the enduring effect of positive lenses; daily brief interruption [1 h] to negative lens (−9.5 D) with positive lenses (+4 D) was effective at inhibiting induced myopia (McBrien et al., 2012). Our results are consistent with these earlier findings; the positive add (generated by the lower negative power zone of bifocal lenses) exerted an enduring restraining influence on eye elongation, over-riding the effect of the single vision negative lenses that were interleaved with the BF lenses. Translated to humans, these results open the possibility that daily bifocal lens-wearing schedules may be reduced in length without significantly compromising their myopia control benefit.

For the interrupted, daily-wear paradigms used in the current study, the BF lenses were always in place at the end of the day, replacing the SV lenses, starting from between 9:30 am and 3:30 pm, according to the protocol (see methods). It is possible that this timing contributed to the very positive outcome of our study. In a study addressing the effect of time of day on the responses to brief defocus exposures, Nickla et al. had young chicks wear +10 D SV lenses for a 2 h period in the morning (5:30 am), noon, or evening (7:30 pm), or wear −10 D SV lenses continuously for 7 consecutive days, except for a 2 h period in the morning or evening. Based on the results of their study, the authors concluded that myopic defocus in the evening was most effective at inhibiting eye growth (Nickla et al., 2017). It is serendipitous that our study design exposed chicks to myopic defocus over the latter period of each day.

In terms of clinical parallels with the treatment paradigm investigated in the current study, it is tempting to draw an analogy with the effect of orthokeratology contact lenses, which are worn at night to allow sharp vision without lenses across the day. Nonetheless, the treatment effect tends to decline across the day, as the cornea recovers from the deformation effect of the lenses (Alharbi and Swarbrick, 2003). As a consequence, less induced peripheral myopic defocus may be experienced towards the end of the day and thus perhaps less myopia control effect may be expected. Do reported differences in the rate of corneal recovery in patients at least partly explain differences in treatment outcomes (Soni et al. 2004; Chen et al. 2010)? Another hint that the effect of the effect of imposed myopic defocus is enduring in humans comes from a 2-year randomized study involving multifocal soft contact lenses designed specifically for controlling myopia progression (DISC lenses)(Lam et al., 2014). The children were recommended to wear their lenses for 5-10 h per day, with the average lens wearing time being ~ 6.5 h per day. The authors report a positive correlation between lens wearing time and treatment effect, with 5 or more hours per day of DISC lens wear linked to ~46% less progression compared to that with SV contact lenses, used as the control treatment in this study. However interpretation of these results is confounded by the use of spectacle lenses in the hours without contact lenses.

While our study suggests the treatment effect to be relatively insensitive to interruption, nonetheless, there is likely to be a daily threshold dose below which we tested and efficacy decreases. The possibility that limiting BF lens treatments to earlier in the day may be less effective also warrants further investigation. Follow-up studies in humans, to directly

examine the influence of bifocal contact lens wear duration and timing on myopia progression are also warranted. The results of our "alternate day" study also predict at least some benefit from part-time bifocal contact lens wear by children, such as instituted to accommodate specific activities, or to simply limit contact lens wear.

The choice of BF lens parameters used in the current study were based on our previous study involving similar 2-zone concentric lens designs, i.e., incorporating different negative power zones (−5 and −10 D), with central zones ranging from 4.5 to 7.5 mm. Our choice of a 4.5 mm central zone diameter for this study reflects the generally greater inhibitory effect on eye elongation for the distance center design included in this previous study, when used either alone or following a 5-day period of myopia induction. In the same study, distance-center lenses tended to out-perform near-center lenses. Such differences are not apparent in the results of the current study, although it may reflect our choice of the alternate day exposure paradigm to compare BFDC and BFNC lenses; the greater reduction in treatment effects with this paradigm is unavoidably linked to reduced sensitivity to detect treatment-related differences. Importantly, in both studies, the placement of all lenses was checked at regular intervals across each day to ensure that they were appropriately centered (Liu and Wildsoet, 2011). Nonetheless, given that the chicks moved their eyes under the lenses, much of the retina would have been exposed to hyperopic and myopic defocus, at least part of the time, with the BF lens designs used.

There was no statistically significant difference between central (on-axis) and peripheral refractions in the 2-zone lens groups. Our previous chick study (Liu and Wildsoet, 2012) that investigated the effect of full-time 2-zone lenses wear without initial induction of myopia found a weak but significant negative correlation between central and peripheral refractions. Specifically, a relative increase in peripheral hyperopia was observed with the 2-zone lens design incorporating a relatively more positive periphery. In the current study in which myopia was induced first, eye shape, as indicated by peripheral versus central refractive errors, did not seem to change, suggesting that changes in eye shape after myopia induction are difficult to reverse. However, the patterns of defocus imposed by concentric bifocal lenses is complicated, as demonstrated for equivalent human contact lenses, which have been shown to alter the eye's spherical aberration and so the plane of best focus with respect to the retina (Tarrant et al., 2008). Similar effects with the lens designs used in the current study can be expected to dilute regional defocus-dependent differences.

In terms of study limitations, we used the chick model to investigate the effect of interrupted wear of 2-zone lenses on myopia progression. Although chicks represent a commonly used myopia model, due to its many advantages, such as rapid eye growth, high sensitivity of refractive state by retinal focus and excellent optics, this model also suffers from the disadvantage of a bilayered, cartilaginous sclera compared to the fibrous only sclera of mammals and primates. Therefore, follow-up studies involving one or both of the latter models would be useful translational steps towards optimizing contact lens-wearing schedules for myopia control in children.

In the current study, we did not investigate the effect of 2-zone concentric lenses when worn for periods shorter than 6 h; however, it seems unlikely that humans would regularly wear

contact lenses for such short periods. Nonetheless, as noted above, the effect of early termination of bifocal lens treatments does warrant investigation in light of the Nickla et al findings related to time-of-day influences on defocus-induced ocular growth effects. Finally, we also did not test the effect of BFNC lens design when worn part-time each day, e.g., 10, 8, or 6 h; this decision on our part reflects the less common clinical use of near center multifocal contact lenses to control myopia progression, although we predict similar effects of reduced wear, as reported here for the BFDC lens design.

Conclusion

This study aimed to characterize the effects of interrupting the daily wear schedule of two-zone concentric bifocal lenses on myopia control treatment efficacy, using the chick myopia model. We conclude that myopia control can still be achieved with bifocal lenses, even when wear is interrupted with up to 6 h per day of SV lens wear. Furthermore, exposure to bifocal lenses every other day still offers some benefit, but is not as effective as full-time myopia control therapy at slowing myopia progression. Our findings open the possibility that daily bifocal lens-wearing schedules may be reduced by up to 50% without substantial reduction in treatment efficacy.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Highlights:

- Myopia control in chicks can still be achieved with bifocal lenses, even when wear is interrupted with up to 6 h per day of SV lens wear.

- Exposure to bifocal lenses every other day still offers some benefit, but is not as effective as full-time myopia control therapy at slowing myopia progression.

- It is possible that daily bifocal lens-wearing schedules may be reduced by up to 50% without substantial reduction in treatment efficacy.
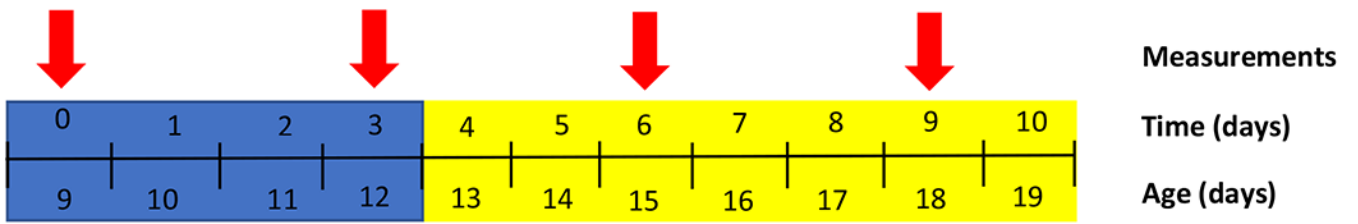
Figure 1:
Schematic summary of the timing of measurements in this study, indicated by red arrows, with respect to the initiation of lens treatments and age of chicks. Yellow highlight is the period when chicks were randomly assigned to one of the seven treatments.
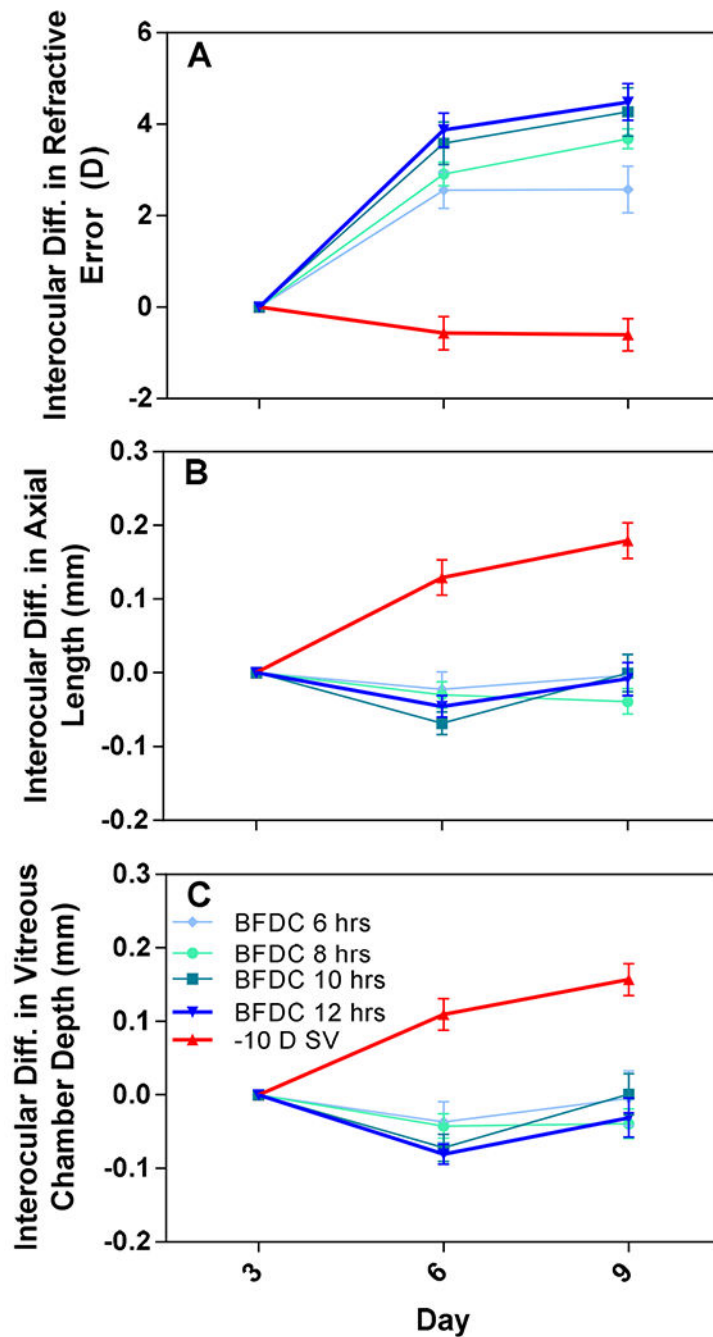
Figure 2:
Interocular differences (mean ± SEM), normalized to day 3 values in (A) spherical equivalent refractive error (D), (B) optical axial length (mm), and (C) vitreous chamber depth (mm) in chicks subjected to the following monocular lens treatments: −10 D SV full-time (12 h) for 9 days (control 1-red), or −10 D SV full-time for 3 days (myopia induction), followed by either BFDC full-time (control 2-dark blue), or BFDC part-time for 10 (turquoise), 8 (light green) or 6 (light blue) h per day, with SV lenses worn for the remainder of each day for 6 days in all cases.
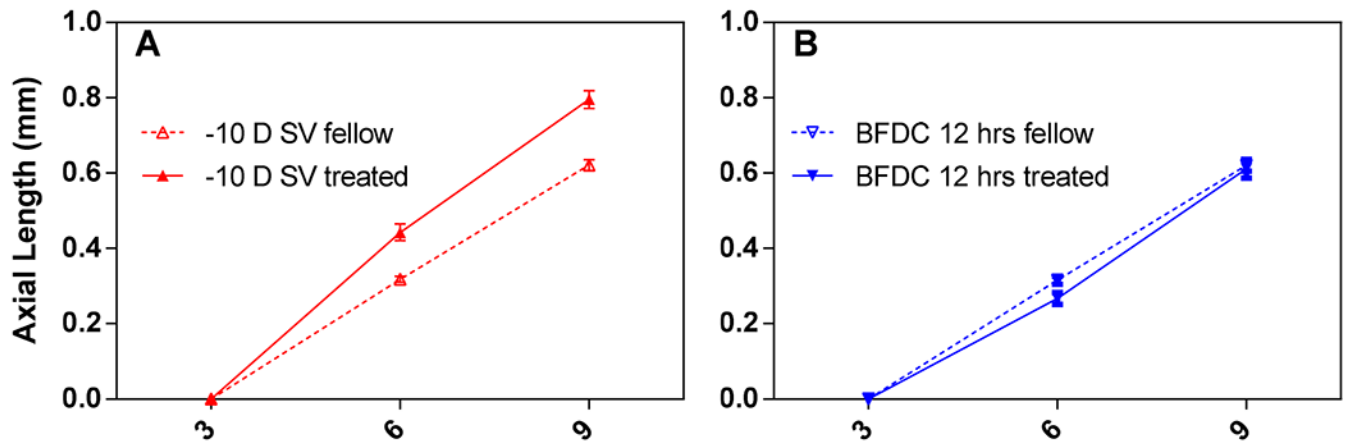
Figure 3:
Axial lengths (mean ± SEM; mm) of treated and fellow eyes, normalized to day 3 values in chicks wearing the following monocular lenses full-time (12 h) for 6 days, either: A) −10 D SV, or B) BFDC, after a 3-day myopia induction period (−10 D SV).
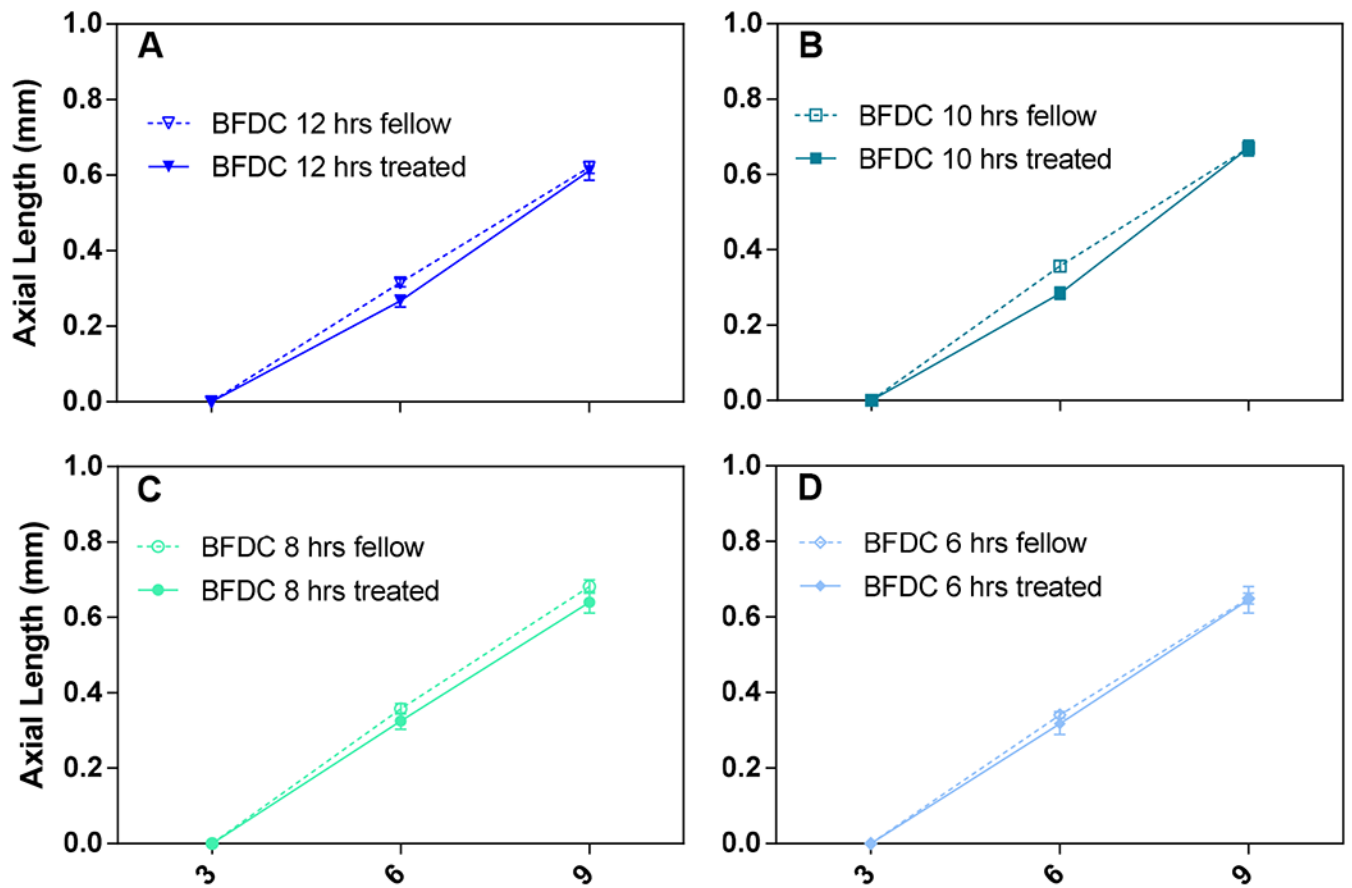
Figure 4:
Axial lengths (mean ± SEM; mm) of treated and fellow eyes, normalized to day 3 values in chicks subjected to the following monocular BFDC lens treatments: A) BF full-time (12 h); B) BF, 10 h; C) BF, 8 h; or D) BF, 6 h; in all cases, there was a 3-day myopia induction period, using −10 D SV lenses, which were also worn over by groups wearing BF lenses parttime, for the remainder of each 12 h day over the 6-day treatment period.
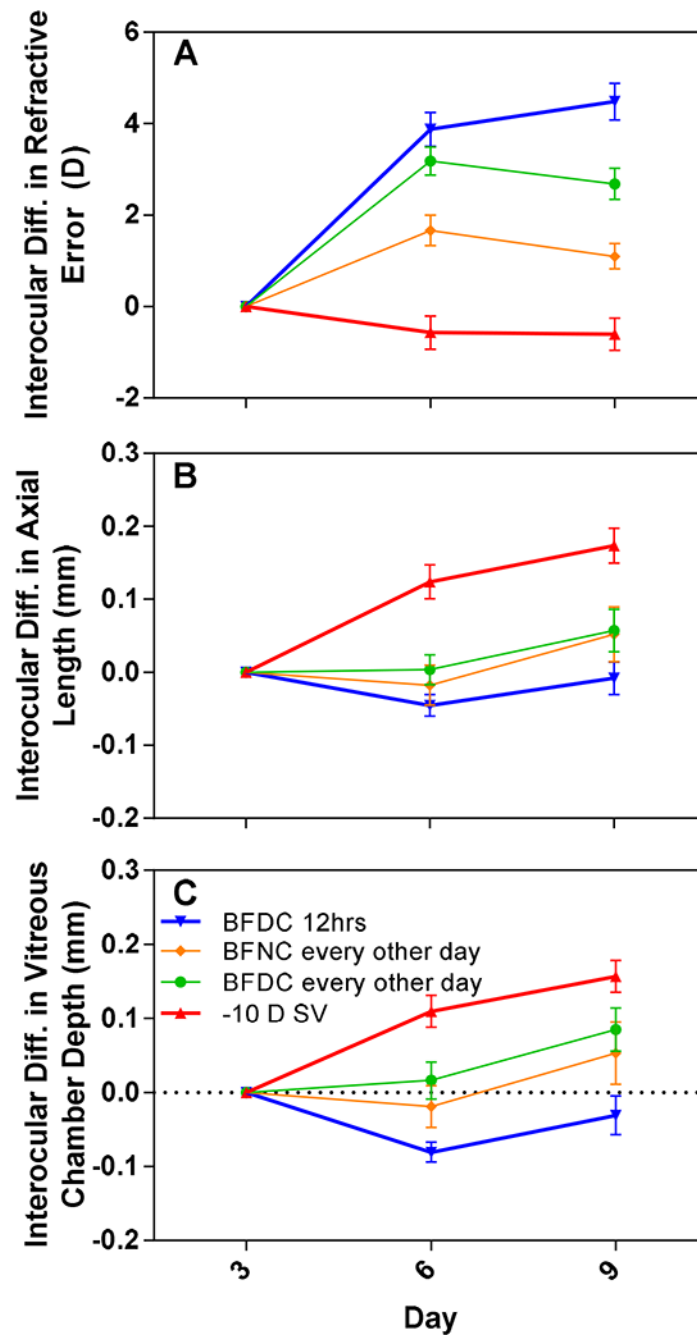
Figure 5:
Interocular differences normalized to day 3 in: (A) spherical equivalent refractive error (D), (B) axial length (mm), and (C) vitreous chamber depth (mm) (mean ± SEM), respectively in chicks subjected to the following monocular lens treatments: 1) −10 D SV (control-red), 2) BFDC full-time (12 h-blue), 3) BFDC alternated every other day with −10 D SV (green), or 4) BFNC alternated every other day with −10 D SV (orange), in all cases for 6 days after a 3-day myopia induction period (using −10 D SV lenses). Data from groups wearing

monocular −10 D SV and BFDC lenses full-time are presented for reference (also presented in Figure 2).
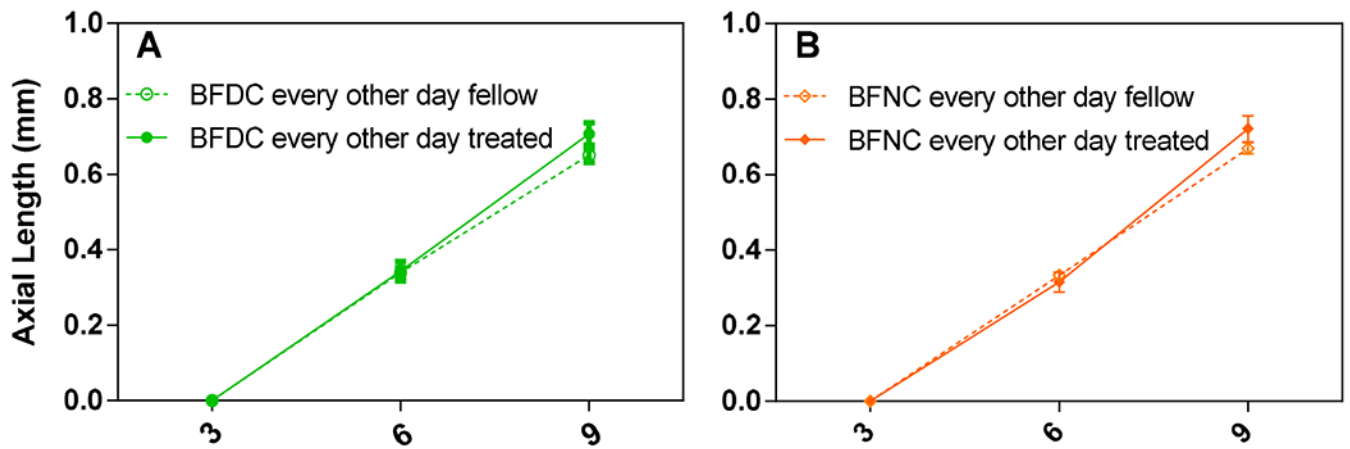
Figure 6:
Axial lengths (mean ± SEM; mm) of treated and fellow eyes normalized to day 3 values in chicks subjected to the following monocular lens treatments: A) BFDC alternated every other day with −10 D SV, or B) BFNC alternated every other day with −10 D SV, in all cases for 6 days after a 3-day myopia induction period.

Table 1:

Details of the monocular lens treatments, including duration of lens wear and group sizes for the seven different treatment groups in the study fitted with monocular −10 D single vision (SV) lenses, worn either full time for 9 days or for 3 days, after which they were interleaved with 2-zone negative lenses as indicated. SV lenses were exchanged for bifocal lenses when the latter were worn only part-time each day (*).

Lens type & hours worn	# of chicks
−10 D SV, 12 h (full-time)	24
−10C/−5P, 12 h (full-time)	16
−10C/−5P, 10 h per day *	15
−10C/−5P, 8 h per day *	14
−10C/−5P, 6 h per day *	14
−10C/−5P, 12 h, every other day*	14
−5C/−10P, 12 h, every other day*	18

C: center; P: periphery

Table 2:

Summary of mean interocular differences in Spherical Equivalent Refractive Error, Optical Axial Length and Vitreous Chamber Depth (± SEM) for seven different treatment groups fitted with monocular −10 D SV lenses, worn either full-time for 9 days or for 3 days, after which they were interleaved with 2-zone negative lenses worn part-time each day, as indicated for additional 6 days.

Treatment Groups	Spherical Equivlent Refractive Error (D)		
	Baseline	Day 3	Day 9
−10D SV 12 h per day	−0.01 ±0.01	−10.05 ±0.42	−10.66 ±0.28
−10/−5D 12 h per day	+0.09 ±0.06	−9.09 ±0.53	−4.61 ±0.29
−10/−5D 10 h per day	+0.05 ±0.09	−9.08 ±0.61	−4.82 ±0.23
−10/−5D 8 h per day	−0.02 ±0.02	−8.89 ±0.32	−5.21 ±0.27
−10/−5D 6 h per day	−0.04 ±0.04	−8.91 ±0.43	−6.34 ±0.34
−10/−5D 12 h every other day	−0.05 ±0.05	−10.98 ±0.23	−8.29 ±0.29
−5/−10D 12 h every other day	−0.01 ±0.01	−9.93 ±0.40	−8.83 ±0.36
Treatment Groups	Optical Axial Length (mm)		
	Baseline	Day 3	Day 9
−10D SV 12 h per day	−0.01 ±0.004	0.24 ±0.02	0.42 ±0.02
−10/−5D 12 h per day	−0.03 ±0.01	0.27 ±0.02	0.26 ±0.02
−10/−5D 10 h per day	−0.03 ±0.01	0.27 ±0.02	0.28 ±0.02
−10/−5D 8 h per day	−0.01 ±0.01	0.28 ±0.03	0.24 ±0.02
−10/−5D 6 h per day	−0.02 ±0.01	0.25 ±0.03	0.25 ±0.03
−10/−5D 12 h every other day	0.00 ±0.00	0.26 ±0.02	0.32 ±0.03
−5/−10D 12 h every other day	−0.01 ±0.01	0.28 ±0.02	0.33 ±0.03
Treatment Groups	Vitreous Chamber Depth (mm)		
	Baseline	Day 3	Day 9
−10D SV 12 h per day	−0.01 ±0.01	0.24 ±0.02	0.40 ±0.02
−10/−5D 12 h per day	−0.02 ±0.01	0.27 ±0.01	0.24 ±0.02
−10/−5D 10 h per day	−0.01 ±0.01	0.28 ±0.02	0.27 ±0.03
−10/−5D 8 h per day	−0.04 ±0.01	0.26 ±0.01	0.22 ±0.03
−10/−5D 6 h per day	−0.003 ±0.01	0.26 ±0.02	0.25 ±0.03
−10/−5D per day 12 h every other day	0.00 ±0.00	0.25 ±0.03	0.27 ±0.02
−5/−10D 12 h every other day	−0.02 ±0.01	0.29 ±0.02	0.27 ±0.02

Table 3:

Summary of mean interocular differences in Choroidal Thickness (± SEM) for the seven different treatment groups fitted with monocular −10 D SV lenses, worn either full time for 9 days or for 3 days, after which they were interleaved with 2-zone negative lenses worn part-time each day, as indicated for additional 6 days.

Treatment Groups	Choroidal Thickness (mm)			
	Baseline	Day 3	Day 6	Day 9
−10D SV 12 h per day	0.002 ± 0.001	−0.053 ± 0.01	−0.014 ± 0.01	−0.024 ± 0.01
−10/−5D 12 h per day	0.04 ± 0.01	−0.08 ± 0.02	0.024 ± 0.03	−0.047 ± 0.02
−10/−5D 10 h per day	0.01 ± 0.009	−0.06 ± 0.01	0.03 ± 0.02	−0.025 ± 0.01
−10/−5D 8 h per day	0.02 ± 0.01	−0.075 ± 0.01	0.06 ± 0.02	−0.01 ± 0.01
−10/−5D 6 h per day	0.008 ± 0.015	−0.10 ± 0.02	0.037 ± 0.03	0.003 ± 0.02
−10/−5D 12 h every other day	0.005 ± 0.005	−0.095 ± 0.03	0.035 ± 0.03	−0.041 ± 0.01
−5/−10D 12 h every other day	0.007 ± 0.004	−0.13 ± 0.02	0.044 ± 0.02	0.01 ± 0.01