A considerable amount of evidence shows that the growth of the eye and the development of refractive error can be modified by changes in visual experience. Lid occlusion and form deprivation in animal models, primarily chicks and monkeys, result in highly myopic refractive errors in a short amount of time.1,2 These animal species are also responsive to the sign and magnitude of defocus created by lenses, compensating for the imposed refractive error by means of accelerated or inhibited ocular elongation.3-5 Animal models have been useful in explaining some aspects of human refractive error development. Disruption of normal, high contrast vision in human infants results in myopic refractive errors.6,7 Human infants are also responsive to their own native hyperopic refractive errors, with modulation of growth that results in near-emmetropia from an axial length well matched to ocular refractive power.8-10

A key feature of the visual control of eye growth is local control, that ocular responses to changes in the visual environment are spatially specific. The portion of the visual field exposed to form deprivation or defocus in animal studies corresponds to the portion of the eye that exhibits the compensating change in growth.11-13 Separating the eye from the central nervous system through optic nerve section does not prevent myopic responses to form deprivation or compensation for refractive errors imposed by minus lenses.12,14 Whereas the central and peripheral retina are both sensitive to changes in the visual environment,11 responses to peripheral manipulations are not always confined to the periphery. The ability of the retinal periphery to alter growth at the fovea has been well documented in foveal ablation experiments in the monkey.15,16 Foveal elongation accelerates when the retinal periphery is preferentially exposed to form deprivation or blur using apertures,15,17 but may not be affected if the exposure is too far into the periphery relative to the central retina.18 Because these studies have only used animal models, the extent of spatial integration of a visual signal by the retinal periphery and its ability to influence foveal growth in children have yet to be determined.

There is good evidence that the peripheral visual environment in children may affect growth at the fovea. Children wearing progressive addition spectacle lenses experience...
less myopia progression. These effects were assumed to be due to reduced hyperopic defocus at the fovea during near vision. However, a report from the Study of Theories about Myopia Progression project suggested that the beneficial effect of progressive addition lenses might be due to superior retinal myopic defocus from the inferiorly placed addition power. Myopia control through center-distance multifocal contact lenses or overnight orthokeratology presents this additional plus power 360° around the periphery. The optical effect of these multifocal contact lenses is to reduce the peripheral hyperopia that is present when children wear a traditional single vision correction, such as glasses or contact lenses. Multifocal contact lens clinical trial results suggest that the influence of the periphery outweighs the local foveal visual signal; despite a clear foveal image and good visual acuity, altering the peripheral optical profile results in slower myopia progression and less axial elongation in children. A theory of growth based on local control would predict that peripheral expansion might be inhibited more than axial elongation during optical myopia control. Different local effects might also be expected between ocular meridians. Baseline results without contact lenses showed that the Bifocal Lenses In Nearsighted Kids (BLINK) study participants had about +1.8 D of relative peripheral hyperopia at 40° in both the nasal and temporal visual fields. Interestingly, the superior and inferior visual fields at 30° showed the opposite sign of defocus, about −0.5 D of relative peripheral myopia. Local control would predict that inhibition of peripheral ocular expansion would be greater in the vertical compared to the horizontal meridian due to greater peripheral myopia. The BLINK study cross-sectional results argue against this meridional local control. Both meridians showed steeper retinas at higher levels of myopia, but the difference between meridians remained similar throughout the range of refractive errors.

The purpose of the current report is to investigate whether the effect of wearing center-distance multifocal soft contact lenses on axial and peripheral elongation of the eye exhibits more local versus global effects compared to single-vision soft contact lenses. Baseline data have been reported previously. The primary analyses in this report address the pattern of inhibition from +2.50 D addition contact lenses compared to +1.50 D addition and single vision contact lenses as a function of retinal meridian, quadrant, and eccentricity using longitudinal data collected over 3 years. Local control of ocular growth would predict that elongation in the vertical meridian would be less than in the horizontal meridian and that peripheral elongation would be inhibited more than axial elongation when wearing +2.50 D addition contact lenses. Similar levels of elongation in both meridians and similar (or greater) inhibition of elongation at the fovea than the periphery would indicate a more global response to wearing multifocal contact lenses.

**METHODS**

Detailed methods used in the BLINK study, and those used for peripheral biometry and refractive error measurements, have been published previously. To summarize, the BLINK study enrolled 294 children between the ages of 7 and 11 years old (inclusive) with between −0.75 D and −5.00 D of myopia in the most hyperopic meridian, less than 1.00 D of astigmatism, and 2.00 D or less of anisometropia into a 3-year randomized clinical trial to determine if center-distance multifocal contact lenses slowed the progression of myopia more than single vision contact lenses. Children were randomized in equal numbers (98 per group) to wear one of three Biofinity soft contact lens designs (CooperVision; Pleasanton, CA): single-vision, multifocal D with +1.50 D addition power, or multifocal D with +2.50 D addition power. The research adhered to the tenets of the Declaration of Helsinki, was reviewed and approved by independent ethical review boards at the University of Houston and The Ohio State University, conformed with the principles and applicable guidelines for the protection of human subjects in biomedical research, and was monitored by an independent data and safety monitoring committee. Consent from children and parental permission were obtained from each participant and participant’s parent/guardian, respectively. The registration for this clinical trial can be found at ClinicalTrials.gov (Identifier: NCT02255474).

All central and peripheral measurements of eye length and refractive error for this report were made on the right eye only under cycloplegia. Subjects received one drop of 0.5% tetracaine or 0.5% proparacaine followed by 2 single drops of 1% tropicamide 5 minutes apart in each eye. Central and peripheral eye length were the average of 5 valid measurements (unflagged by the instrument) at each retinal location using the Lenstar LS 900 optical biometer (Haag-Streit USA, Mason, OH). Axial length was measured along the line of sight, then peripheral eye length was measured by having the subject turn the eye to fixate small targets on the face of the instrument at eccentricities of 20° and 30°, both horizontally in nasal and temporal gaze and vertically in superior and inferior gaze. Central and peripheral refractive error were measured with and without contact lens correction using the open-view Grand Seiko WAM-5500 binocular autorefractor/keratometer (AIT Industries, Bensenville, IL). The central value was the average of 10 valid readings, whereas the peripheral values were the average of 5 valid readings (within ±1.0 D of the median value for sphere and cylinder). Central refractive error was measured along the line of sight, then horizontal peripheral refractive error was measured in nasal and temporal gaze at eccentricities of 20°, 30°, and 40°. Vertical peripheral refractive error was measured in superior and inferior gaze at 20° and 30°. Measurements of peripheral refractive error with the contact lenses in place were only made in the horizontal meridian because contact lens decentration could be avoided by having participants turn their head laterally during measurement instead of their eyes; this was not possible for vertical measurements. Peripheral refraction in the vertical meridian with contact lenses in place was estimated under an assumption of rotational symmetry. The differences in peripheral measurements between eye-only and the eye wearing a lens at each horizontal eccentricity were added to the corresponding eye-only values at each vertical eccentricity. Statistical analyses were completed using SAS, version 9.4 for Windows (SAS Institute, Cary, NC). The modeled 3-year changes in elongation at 20° and 30° were analyzed by treatment group and within each of the 4 quadrants. The modeled 3-year change in axial elongation was compared to peripheral elongation, again by treatment group and within each of the 4 quadrants. In order to avoid the many comparisons generated by multiple eccentricities, and to create analyses similar to those for baseline data, individual participant peripheral eye length data were also fit by quadratic equations as a function of gaze angle, one horizontal and one vertical, for each study year. This approach has been used for peripheral biometry and refractive error measurements.
validated against magnetic resonance imaging (MRI) and schematic eye retinal contours.\textsuperscript{27-29} Models for each of these analytic approaches included treatment group, study year (categorical variable), and their interactions adjusted for sex, age group, and study site. The \( P \) values for eccentricity and quadrant comparisons were adjusted for multiple comparisons using the step-down Bonferroni method of Holm.\textsuperscript{30}

**RESULTS**

As previously reported for the BLINK study, approximately 60\% of the participants were girls, the average age was 10.3 ± 1.2 years, 60\% were 10 or 11 years old at baseline, 26\% were Hispanic or Latino, and 68\% were White.\textsuperscript{24} The average baseline cycloplegic refractive error was \(-2.39 \pm 1.00 \) D with only small amounts of astigmatism (average ± standard deviation: \( J_0 = +0.06 \pm 0.19 \) D; \( J_45 = +0.05 \pm 0.14 \) D). Of the 294 enrolled subjects, 287 (97.6\%) completed the 3-year visit. The multifocal addition power resulted in a different peripheral refractive error profile at the baseline visit compared to wearing single vision contact lenses. The +2.50 D addition power decreased peripheral hyperopia in the horizontal meridian seen with single vision contact lenses, resulting in small amounts of peripheral myopia across ±30° but not at 40° for either the nasal or the temporal retina. The +2.50 D addition power increased the estimated amount of peripheral myopia in the vertical meridian compared to single vision contact lenses. Peripheral refractive error for the +1.50 D addition power was intermediate between the +2.50 D addition power and single vision contact lenses (Fig. 1).

Randomization resulted in balanced peripheral eye lengths between treatment groups with no significant differences at baseline at any corresponding quadrant or eccentricity (All \( P > 0.37 \)). Eyes elongated each year at every measured eccentricity in both meridians and in all three treatment groups. The pattern of elongation kept the peripheral eye length profile generally parallel to the profile at baseline (Fig. 2). Changes in foveal and peripheral eye length during each study year are depicted in Supplementary Figure S1. This general symmetry in elongation can be seen in the similar amounts of change across eccentricities between each study year and in each meridian. Figure 2 and Supplementary Figure S1 also illustrate the inhibition in elongation produced by wearing +2.50 D addition contact lenses compared to +1.50 D addition and single vision contact lenses. The pattern of inhibition across ±30° of the retina also appears to be generally symmetric, with a parallel but lower amounts of change across the retina, particularly between baseline and year 1, for the compressed pattern for eye lengths in both meridians (Figs. 2A, 2B) and lower amounts of change across the retina, particularly between baseline and year 1 (Supplementary Figs. S1A, S1B), for the +2.50 D addition multifocal contact lenses than +1.50 D addition and single vision contact lenses (Supplementary Figs. S1A, S1B).

The results for elongation at the fovea of the right eye only in this report are similar to those previously reported for both eyes: children randomized to wearing +2.50 D addition contact lenses had less axial elongation over 3 years (0.39 mm, 95\% confidence interval [CI] = 0.33 to 0.46 mm) than those wearing either +1.50 D addition (0.55 mm, 95\% CI = 0.47 to 0.63 mm) or single vision contact lenses (0.63 mm, 95\% CI = 0.57 to 0.70 mm; \( P < 0.001 \) for comparisons between +2.50 D addition and either +1.50 D addition or single vision control).\textsuperscript{24} The +2.50 D addition had its greatest effect in year 1 when eye growth was most rapid (\( P < 0.001 \)) and continued to significantly inhibit elongation in year 2 (\( P < 0.001 \)). However, there was no significant difference in the rate of axial elongation between treatment groups in year 3 (\( P = 0.59 \)).

The cumulative 3-year changes in eye length again showed generally symmetric elongation with overlapping 95\% CIs across the retinal eccentricities within a quadrant and treatment group (Fig. 3). These similar rates of elongation occurred despite baseline horizontal and vertical asymmetries. Eye length in the temporal retinal quadrant was already relatively shorter at baseline by 0.40 mm at 30° than the nasal retinal quadrant (Fig. 2A) and eye length in the inferior retinal quadrant was 0.15 mm

![Figure 1](image-url)  
**Figure 1.** Peripheral refractive error with contact lenses in place at the baseline visit (single vision, +1.50 D addition power, and +2.50 D addition power) in (A) the horizontal meridian, and (B) estimated values for the vertical meridian. Error bars represent the standard error of the mean (some obscured; vertical standard errors estimated from vertical peripheral refraction).
shorter at $+30^\circ$ than the superior retinal quadrant at $-30^\circ$ (Fig. 2B). Although elongation was generally symmetric within a treatment group, statistically significant interactions between treatment group and both quadrant (interaction $P = 0.005$) and eccentricity (interaction $P = 0.0002$) indicated that treatment resulted in small, but important, departures from this symmetry. For children wearing single vision contact lenses, elongation was greater at $20^\circ$ than at $30^\circ$ in 3 out of 4 quadrants by an average of 0.05 mm (95% CI = 0.03 to 0.08 mm; $P < 0.001$; Figs. 3A, 3C, 3D). Only the temporal quadrant had similar amounts of elongation at $20^\circ$ and $30^\circ$ (Fig. 3B). Axial elongation was greater than peripheral elongation in the superior and temporal quadrants (axial-superior = 0.07 mm [95% CI = 0.05 to 0.09 mm; $P < 0.001$]; axial-temporal = 0.06 mm [95% CI = 0.03 to 0.09 mm; $P = 0.002$]; Figs. 3B, 3C). Axial and peripheral elongation were similar in the inferior and nasal quadrants (Figs. 3A, 3D). This pattern with single vision contact lenses was similar in children wearing $+1.50$ D addition contact lenses. There were no significant differences in elongation at either $20^\circ$ or $30^\circ$ in either meridian between children wearing $+1.50$ D addition power and those wearing single vision contact lenses. Axial elongation was again greater than peripheral elongation in the superior and temporal quadrants and similar to each other in the inferior and nasal quadrants (axial-superior = 0.04 mm [95% CI = 0.02 to 0.06 mm; $P = 0.008$]; axial-temporal = 0.08 mm [95% CI = 0.05 to 0.11 mm; $P < 0.001$]). Compared to wearing single vision lenses, children wearing $+2.50$ D addition multifocal contact lenses showed significantly less elongation at all corresponding peripheral points by 0.16 to 0.28 mm ($P < 0.001$ to 0.049) with the exception of $30^\circ$ in the superior retina (Fig. 3C). The largest effects of treatment with $+2.50$ D multifocal contact lenses occurred at $20^\circ$ and the fovea. The significant differences in elongation between $20^\circ$ and $30^\circ$ with single vision lenses were not present with $+2.50$ D addition multifocal contact lenses. Axial elongation was similar to peripheral elongation in the superior quadrant and less than peripheral elongation in the inferior and nasal quadrants, neutralizing or reversing the pattern seen with single vision contact lenses (axial-inferior = $-0.04$ mm [95% CI = $-0.06$ to $-0.01$ mm; $P = 0.051$]; axial-nasal = $-0.06$ mm [95% CI = $-0.09$ to $-0.02$ mm; $P = 0.005$; Figs. 3A, 3C, 3D). Only the temporal quad-

**Figure 2.** Eye lengths measured across $\pm 30^\circ$ of the (A) horizontal meridian and (B) vertical meridian in each year of the study. Error bars represent standard errors of the mean.
Three-year changes in eye length by eccentricity and retinal/visual field quadrant. Error bars represent the 95% confidence interval.

The results based on quadratic fits to the peripheral eye length profiles of individual participants were consistent with those above by eccentricity and quadrant. A negative quadratic coefficient in Figure 4A indicates a downward-turned parabola, with more negative values associated with steeper retinas (i.e. shorter eye length with greater eccentricity). As previously reported, coefficients at baseline were more negative in the horizontal meridian than in the vertical meridian.25 The quadratic coefficients for eye length profile for children wearing single vision contact lenses became more negative over the 3 years of the study in both the horizontal (P < 0.003) and the vertical meridians (P < 0.001; Fig. 4A), consistent with greater axial than peripheral elongation noted above. Axial elongation at the fovea when wearing single vision contact lenses was 0.63 mm, greater than the quadratic model estimates of peripheral elongation at 30° in the superior (0.54 mm) and temporal (0.56 mm) retinal quadrants and similar to foveal elongation in the nasal and inferior retina (0.61 mm; Fig. 5). In contrast to the pattern seen with single vision contact lenses, the quadratic coefficients for the +2.50 addition group either underwent no significant change over 3 years in the horizontal meridian (P = 0.42) or became less negative in the vertical meridian (P = 0.006). Results for the +1.50 D addition group were intermediate, with no significant change in the quadratic coefficients in either meridian (all P > 0.06). Inhibition of elongation with +2.50 D addition contact lenses was most often greatest at the fovea. The treatment effect (estimated by the difference between the green and the blue curves in Fig. 5) was 0.24 mm at the fovea, but only 0.12 mm, 0.14 mm, and 0.16 mm at 30° in the superior, nasal, and inferior quadrants, respectively. The effect of treatment was only similar to that at the fovea at 30° in the temporal retina (0.22 mm; Fig. 5A). These results suggest that wearing +2.50 addition multifocal contact lenses neutralized the pattern of increasing retinal steepness seen with single vision contact lenses in the horizontal meridian and reversed it in the vertical meridian toward becoming flatter.

The asymmetry in eye length profile is described by the linear term of the quadratic fit. The linear coefficient...
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FIGURE 4. (A) Average quadratic coefficients fit to eye length data across ±30° of the retina in the horizontal and vertical meridian by treatment group and study year. Error bars represent 95% confidence intervals. (B) Average linear coefficients from the quadratic equations fit to eye length data across ±30° of the retina in the horizontal and vertical meridian by treatment group and study year. Error bars represent 95% confidence intervals.

cients were consistent with the nasal-temporal and superior-inferior asymmetries noted above at baseline (Fig. 4B). The negative value in each meridian indicates a shorter eye length in the temporal and inferior retinal quadrants, respectively. The linear terms showed significant changes in the negative direction over the 3 years of the study in the horizontal meridian in all 3 treatment groups \((P < 0.008)\) and in the positive direction in the vertical meridian for children wearing single vision \((P < 0.001)\) and +1.50 D addition contact lenses \((P = 0.005)\). The linear coefficient for the vertical meridian showed no significant change over 3 years in children wearing the +2.50 D addition multifocal contact lenses \((P = 0.14)\).

DISCUSSION

The eyes of children wearing single vision contact lenses for 3 years elongated more at the fovea than in the periphery, resulting in a steeper retina than at baseline. The eyes of children wearing +2.50 D addition center-distance contact lenses showed either similar or less elongation at the fovea compared to the periphery in 3 of the 4 measured quadrants. As a result, the retinal steepening seen with single vision contact lenses was either not observed in the horizontal meridian or reversed toward a flatter retina than at baseline. The report most relevant to the BLINK study is from a recent study of 58 myopic Chinese children 8 to 12 years of age who self-selected to be fit with either overnight orthokeratology or single vision spectacles for 1 year. The eye elongated at the fovea and at all peripheral points in the single vision spectacle group, as expected. Elongation in the orthokeratology group was unexpectedly greater for the nasal than with single vision spectacles, and by a substantial amount in one year of up to 0.21 mm. The BLINK study also showed greater inhibition of elongation in the temporal compared to the nasal retina, but there was evidence of inhibition of elongation at the most peripheral points including nasally, even after 1 year. Peripheral elongation was never greater in children wearing +2.50 D addition contact lenses than with single vision lenses. Both orthokeratology and the center-distance multifocal contact lenses used in the BLINK study (Fig. 1) expose the peripheral retina to myopic defocus, making it difficult to pinpoint the reason for the difference between the results for the two studies.

There are few longitudinal studies of peripheral eye length to compare to the BLINK study results. A study of 140 mostly emmetropic children also found elongation in all 4 retinal quadrants at 20° after 30 months of follow-up. Greater foveal than peripheral elongation found in the current study aligns well with a cross-sectional result from MRI scans showing that axial length exceeds eye width and height, and by greater amounts at higher amounts of myopia. The report most relevant to the BLINK study is from a recent study of 58 myopic Chinese children 8 to 12 years of age who self-selected to be fit with either overnight orthokeratology or single vision spectacles for 1 year. The eye elongated at the fovea and at all peripheral points in the single vision spectacle group, as expected. Elongation in the orthokeratology group was unexpectedly greater for the nasal retina than with single vision spectacles, and by a substantial amount in one year of up to 0.21 mm. The BLINK study also showed greater inhibition of elongation in the temporal compared to the nasal retina, but there was evidence of inhibition of elongation at the most peripheral points including nasally, even after 1 year. Peripheral elongation was never greater in children wearing +2.50 D addition contact lenses than with single vision lenses. Both orthokeratology and the center-distance multifocal contact lenses used in the BLINK study (Fig. 1) expose the peripheral retina to myopic defocus, making it difficult to pinpoint the reason for the difference between the results for the two studies.

The peripheral optical profiles of single vision and +2.50 D addition contact lenses were asymmetric by both quadrant and eccentricity (Fig. 1), providing an opportunity to evaluate global versus local responses to defocus. Single vision contact lenses were associated with large and nearly equal amounts of peripheral hyperopia in both nasal and temporal horizontal quadrants, whereas the vertical meridian was consistently emmetropic. Therefore, local control of eye growth by defocus would not explain the nasal-temporal asymmetry in elongation nor the generally symmetric pattern of elongation between the horizontal and vertical meridians with single vision lenses. The +2.50 D addition reduced peripheral hyperopia in the horizontal meridian, particularly at 20° over the temporal retina, and produced a substantial amount of peripheral myopia.
in the vertical meridian (Fig. 1). This altered profile was associated with a positive treatment benefit of reduced elongation across the ±30° of the retina in all quadrants. However, local defocus would not explain the lower degree of inhibition of elongation peripherally in three of the four quadrants compared to the fovea, the portion of the retina with the least change in its image. Local defocus would also not explain the similar amounts of inhibition between the horizontal and vertical ocular meridians. Local control of ocular growth would be more consistent with less elongation in the vertical than the horizontal meridian and greater inhibition of peripheral than axial elongation. Given that these two outcomes did not occur in the BLINK study, the eye seems to exhibit a more global than local response to the optical profile created by the +2.50 D multifocal contact lenses.

Local defocus cues might still be the effective signal but perhaps are being integrated over an extensive amount of the peripheral retina. Another possibility to explore is that similar growth between meridians may be the result of reduced sensitivity in the vertical meridian to inhibition by peripheral myopia because of its habitual exposure to that sign of defocus. The global response seems more similar to an emmetropic pattern of elongation, namely more symmetric change between fovea and periphery as opposed to the greater axial than the peripheral elongation seen during myopic progression with standard single vision corrections. Uniformity of change between the fovea and periphery as measured by eye length or peripheral refraction is seen in children likely to remain emmetropic. This pattern may also be characteristic of a positive treatment effect during myopia control. The 2-year results for children wearing Defocus Incorporated Multiple Segments (DIMS) lenses showed a more uniform pattern of change in peripheral refraction than single vision lenses across the horizontal ±30° of the retina. The recent study of peripheral eye lengths following orthokeratology also found that the pattern of growth was more symmetric across the retina than with single vision glasses. It should be recognized that this slower growth during myopia control is still much faster than would be expected in 7 to 11 year old emmetropic children. Axial elongation over 3 years from the age of 10 to 13 years might be 0.20 to 0.22 mm in children without myopia compared to 0.39 mm seen in the BLINK study participants wearing +2.50 D addition contact lenses. Current approaches to myopia control may change the pattern and
rate of eye elongation, but more successful myopia control should have even greater levels of inhibition as a goal. Greater levels of inhibition across the retina would also be worthwhile. The differences in elongation between +2.50 D addition contact lenses and single vision contact lenses were less peripherally than at the fovea by as much as 50%, or 0.12 mm in the superior retina compared to the 0.24 mm of treatment effect seen at the fovea. This result suggests the need to evaluate elongation at locations more peripheral than 30°. The ±30° retinal eccentricity corresponds to a sagittal depth of about 2 to 3 mm within a vitreous chamber that might be 17 mm deep in a young, myopic eye. Current optical biometric techniques for measuring eye length cannot assess more extreme eccentricities, leaving most of the retinal periphery unmeasured. Inhibition of elongation should extend throughout the entire retinal periphery if myopia control truly results in a smaller globe than an untreated eye. A large part of the motivation for initiating myopia control is because the increasing prevalence of myopia is expected to increase ocular morbidity from excessive eye enlargement.43-45 The axial benefit of myopia control loses considerable value if it does not result in an overall smaller eye.

Conclusions

Wearing multifocal contact lenses with a +2.50 D addition reduced that rate of elongation at every peripheral point in a generally global, symmetric pattern. However, the presence of minor deviations from completely symmetric inhibition of elongation has important implications. Foveal and peripheral eye elongation did not follow the pattern predicted by local defocus cues. Less elongation in the vertical meridian than the horizontal and less elongation peripherally than axially were not observed. The degree of inhibition of elongation was similar between the horizontal and vertical meridians and greater at the fovea than in the periphery when wearing +2.50 D center-distance multifocal contact lenses. If local control does not explain the more global response of the eye to multifocal contact lenses, future research should attempt to better characterize the optical signals and ocular mechanisms that are responsible for the treatment benefit produced by this form of myopia control. Assessments of elongation beyond 30° during myopia control are also needed.

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