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Optical treatment strategies to slow myopia progression: Effects of the visual extent of the optical treatment zone

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ABSTRACT

In order to develop effective optical treatment strategies for myopia, it is important to understand how visual experience influences refractive development. Beginning with the discovery of the phenomenon of form deprivation myopia, research involving many animal species has demonstrated that refractive development is regulated by visual feedback. In particular, animal studies have shown that optically imposed myopic defocus slows axial elongation, that the effects of vision are dominated by local retinal mechanisms, and that peripheral vision can dominate central refractive development. In this review, the results obtained from clinical trials of traditional optical treatment strategies employed in efforts to slow myopia progression in children are interpreted in light of the results from animal studies and are compared to the emerging results from preliminary clinical studies of optical treatment strategies that manipulate the effective focus of the peripheral retina. Overall, the results suggest that imposed myopic defocus can slow myopia progression in children and that the effectiveness of an optical treatment strategy in reducing myopia progression is influenced by the extent of the visual field that is manipulated.

Myopia is a significant public health issue. In East Asia, where the prevalence of myopia has reached epidemic proportions (Lin et al., 1999; Saw et al., 1996), the ocular morbidity associated with the exaggerated axial growth that produces the most common forms of myopia is a leading cause of permanent vision disability (Liu et al., 2001; Saw et al., 2005). Unfortunately, the prevalence of myopia, and particularly high degrees of myopia, are continuing to increase in the urban areas of Asia (Lin et al., 2004) and recent evidence indicates that a similar trend is occurring in the USA (The Framingham Offspring Eye Study Group, 1996; Vitale et al., 2008) and other non-Asian countries (Bar Dayan et al., 2005; Rose et al., 2001).

Myopia usually manifests in childhood (most often between the ages of 7–10 years in the USA; Hirsch, 1952; Young et al., 1954) and the degree of myopia typically continues to increase in magnitude over a period of years (Goss and Winkler, 1983). Because the personal and societal burdens of myopia increase with the degree of myopia (Saw et al., 2005), treatment strategies that can eliminate or reduce the progression of myopia would have significant benefits. As a consequence, substantial effort has been devoted to developing treatment regimens that are effective in reducing myopia progression (for a recent review see Walline et al., 2011b).

To date, pharmaceutical strategies that employ muscarinic cholinergic receptor blockers have been the most effective treatment strategies for childhood myopia. Specifically, topically applied atropine, a powerful muscarinic antagonist, has been shown to reduce myopia progression in children by more than 70% over a two-year treatment period (Chua et al., 2006; Shih et al., 1999). It is clinically significant that these reductions in myopia progression were due to reduced axial elongation rates. Although atropine and other muscarinic agents (e.g., pirenzephine) can slow myopia progression, concerns about post-treatment rebound effects (Tong et al., 2009) and the short- (Chua et al., 2006; Shih et al., 1999) and long-term side effects (Smith et al., 1984) associated with prolonged treatment courses have discouraged the widespread use of these drugs. However, recent studies have shown that very low doses of atropine (e.g., 0.01% versus the more typical concentrations of 0.5% or 1.0%) can also produce meaningful reductions in myopia progression (Chia et al., 2011), which may mitigate some of these concerns.

Regardless, it would be advantageous to develop a variety of treatment options to reduce myopia progression, particularly optical strategies that can be readily incorporated into the spectacles

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and contact lenses that are normally employed in children to correct the optical consequences of myopia on distance vision. With respect to optical treatment strategies, three observations in laboratory animals provide a rationale for potential optical treatment strategies. First, animal studies have demonstrated that refractive development and axial growth are regulated by visual feedback associated with the eye's effective refractive status, in essence optical defocus. In particular, lens compensation experiments have shown that optically imposed myopic defocus can slow axial growth (Howlett and McFadden, 2009; Hung et al., 1995; Schaeffel et al., 1988; Siegwart and Norton, 2010; Smith and Hung, 1999; Whatham and Judge, 2001). Second, the dominant effects of vision on refractive development are mediated by local retinal mechanisms that operate in a regionally selective manner (Smith et al., 2009a; Smith et al., 2010; Wallman et al., 1987). As a consequence, visual signals in the periphery can influence ocular shape and axial length in a manner that is independent of central vision. The fact that it is possible to alter vitreous chamber elongation and refractive error in a localized manner also rules out many of the global mechanisms that have historically been hypothesized to influence myopia progression (e.g., the act of accommodation). And third, although it is logical to expect visual signals from the fovea to dominate visually guided refractive development (Stone and Flitcroft, 2004), peripheral vision and the peripheral retina can, probably as a result of areal summation effects (Wallman and Winawer, 2004), have a substantial influence on overall ocular growth and central refractive development (Liu and Wildsoet, 2011, 2012; Smith et al., 2009b; Smith et al., 2005). Although the manner in which signals are integrated across the retina, i.e., across local retinal mechanisms, is largely unknown, optical treatment strategies that take into account the periphery are more likely to be successful than those that ignore the optical state of the periphery.

Traditional optical treatment strategies, which have been designed to primarily manipulate central vision, have been shown to significantly alter ocular growth and refractive development in children. However, with most of these strategies the reductions in myopia progression have been modest and in one case the intervention actually appears to have increased myopia progression. In this review, the results for these traditional strategies are 1) interpreted in light of the results from animal studies and 2) compared to the results reported in recent, but largely preliminary studies that have investigated the efficacy of optical treatment regimens that manipulate retinal imagery over a relatively large proportion of the retina. The trend across studies suggests that imposed myopic defocus can slow myopia progression and that the effectiveness of an optical treatment strategy in reducing myopia progression is influenced by the extent of the visual field that is manipulated.

1. Undercorrection versus full-correction spectacles

The finding that optically imposed myopic defocus slows axial growth in animals suggests that myopia in children should be self-limiting. If the refractive error is left uncorrected, progression should not occur. Similarly, at first glance, the results from animal studies imply that undercorrecting myopic eyes, i.e., prescribing spectacles for distance vision that do not fully correct the manifest myopic refraction, should slow myopia progression. Interestingly, the two recent studies that have examined the effects of undercorrection versus full-correction spectacles report that undercorrection may actually increase myopia progression. Fig. 1 illustrates the relative myopia progression in subjects who wore full corrections versus individuals who were undercorrected by either 0.50 (Adler and Millodot, 2006) or 0.75 D (Chung et al., 2002). At the end of the first year of treatment, the 72 subjects in the undercorrected groups had, on average, progressed 0.17 D more than the 70 subjects in the full-correction groups. The Chung et al. study was halted at 2 years because myopia progression was significantly higher in the undercorrected subjects than in the control subjects (0.23 D) and the 30% higher progression rates were associated with faster axial elongations rates.

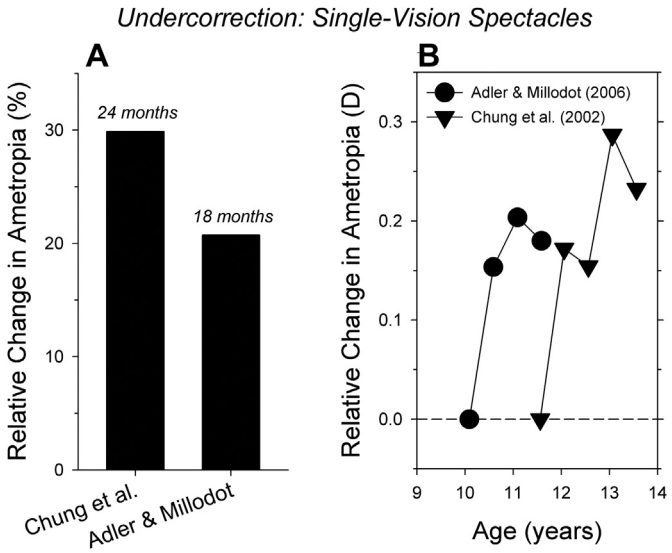

Fig. 1. A. Average relative changes in refractive error obtained at the end of the treatment period in undercorrected myopic subjects and control subjects prescribed traditional full myopic corrections (percentage: treated − control/control). Positive values indicate that the treated, undercorrected subjects exhibited larger myopic shifts than the controls subjects. B. Average differences in refractive error (diopters: control group − treated group) plotted as a function of time from the onset of treatment. The first symbol for each study reflects the average age of the subjects in the treated group. All of the subjects wore single vision lenses. The data were replotted from Adler and Millodot (2006) and Chung et al. (2002).

It has been argued that the pattern of results obtained with undercorrection strategies cast doubt on whether the results of animal studies can be applied to children (e.g., Adler and Millodot, 2006). However, it is important to recognize that the conditions created by undercorrecting myopic children are not necessarily the same as those produced by optically imposed myopic defocus in normal infant animals. When similar optical conditions are produced in children and animals, the effects of the visual manipulations on refractive development have been consistent. For example, conditions like form deprivation that eliminate meaningful visual feedback consistently result in unregulated/un-dampened axial growth and relative myopic shifts in refractive error in both children (Rabin et al., 1981) and animals (Smith et al., 1987; Wiesel and Raviola, 1977). More importantly, optically imposed defocus produces similar compensating alterations in the refractive errors of children and animals. For instance, monovision correction strategies that impose myopic anisometropia that is very consistent over time produce compensating anisometropic changes in children (Phillips, 2005) that are qualitatively similar to those produced by optically imposed anisometropia in monkeys (Smith and Hung, 1999). One reason that the similarities between humans and animals are more obvious with these anisometropic rearing regimens is that regardless of the viewing distance the imposed anisometropia is always present and the viewing conditions in animals and humans are very similar.

Why does undercorrection fail to slow myopia progression? It has been suggested that the vision-dependent mechanisms that regulate refractive development in myopic children may not be able to accurately detect the sign of defocus, i.e., the mechanisms that mediate emmetropization are not functioning properly (Chung et al., 2002). In this respect, it has recently been reported that in