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Interocular suppression in children with deprivation amblyopia

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ABSTRACT

In patients with anisometropic or strabismic amblyopia, interocular suppression can be minimized by presenting high contrast stimulus elements to the amblyopic eye and lower contrast elements to the fellow eye. This suggests a structurally intact binocular visual system that is functionally suppressed. We investigated whether suppression can also be overcome by contrast balancing in children with deprivation amblyopia due to childhood cataracts. To quantify interocular contrast balance, contrast interference thresholds were measured using an established dichoptic global motion technique for 21 children with deprivation amblyopia, 14 with anisometropic or mixed strabismic/anisometropic amblyopia and 10 visually normal children (mean age mean = 9.9 years, range 5–16 years). We found that interocular suppression could be overcome by contrast balancing in most children with deprivation amblyopia, at least intermittently, and all children with anisometropic or mixed anisometropic/strabismic amblyopia. However, children with deprivation amblyopia due to early unilateral or bilateral cataracts could tolerate only very low contrast levels to the stronger eye indicating strong suppression. Our results suggest that treatment options reliant on contrast balanced dichoptic presentation could be attempted in a subset of children with deprivation amblyopia.

1. Introduction

Abnormal visual experience during childhood can result in amblyopia, a neurodevelopmental disorder of the visual system (Birch, 2012). There are three primary causes of amblyopia; anisometropia (a difference in refractive error between the eyes, causing chronic image blur in one eye), strabismus (ocular misalignment, causing a decorrelation of the images seen by each eye) and deprivation (physical obstruction of vision in one or both eyes) (Holmes & Clarke, 2006). Visual deprivation is most often caused by childhood cataract (an opacification of the lens), a rare and serious condition, requiring surgical removal of the opaque lens, and extensive post-operative care (Medsinge & Nischal, 2015; Oscar, Veleva, Chernodrinska, Kemilev, & Petkova, 2014; Repka, 2010).

The hallmark of amblyopia is reduced visual acuity in an otherwise healthy eye after full correction of amblyogenic factors. There is a strong evidence base for the use of refractive correction (Cotter, 2006; Cotter et al., 2012; Stewart, Moseley, Fielder, & Stephen, 2004) and either occlusion or penalization of the fellow eye (Repka et al., 2014; Wallace et al., 2011, 2013) to treat the visual acuity deficit in children with strabismic or anisometropic amblyopia. However, evidence from randomized clinical trials supporting the use of patching or penalization to treat deprivation amblyopia is lacking (Antonio-Santos, Vedula, Hatt, & Powell, 2014; Hatt, Antonio-Santos, Powell, & Vedula, 2009).

In addition to the loss of visual acuity, many other monocular and binocular visual deficits have been associated with amblyopia including impairments in Vernier acuity, stereopsis, contrast sensitivity and global motion perception (see Asper, Crewther, & Crewther, 2000; Hamm, Black, Dai, & Thompson, 2014 for reviews). The extent to which the effects of deprivation amblyopia differ from anisometropic or strabismic amblyopia remains an open question, because the majority of psychophysical amblyopia studies have included either anisometropic and strabismic amblyopia, *or* deprivation amblyopia (McKee, Levi, & Movshon, 2003 is a

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notable exception). The most severe forms of deprivation amblyopia are caused by cataracts that restrict patterned visual input from birth or during early infancy. It is conceivable that this very early and complete visual deprivation has a different effect on visual development than strabismus or anisometropia. There are data that indirectly support this hypothesis. For example, deprivation amblyopia caused by congenital cataract is typically associated with greater losses in contrast sensitivity (Birch, Stager, Leffler, & Weakley, 1998; Levi & Harwerth, 1978;Tytla, Maurer, Lewis, & Brent, 1988), stereopsis (Greenwood et al., 2012; Hartmann et al., 2015; Ing, 2011; Wallace et al., 2011), and global motion perception (Constantinescu, Schmidt, Watson, & Hess, 2005; Ellemberg, Lewis, Maurer, Brar, & Brent, 2002; Hadad, Maurer, & Lewis, 2012) than have been reported for other subtypes of amblyopia (reviewed by Hamm et al., 2014).

Furthermore, whereas strabismic and anisometropic amblyopia are typically unilateral, deprivation amblyopia can be unilateral or bilateral (Holmes & Clarke, 2006). In fact, deprivation amblyopia caused by childhood cataract is bilateral in just over half of all cases (Rahi & Dezateux, 2000; Wirth et al., 2002). Unilateral and bilateral deprivation amblyopia have different effects on visual function. For example, unilateral deprivation amblyopia results in more severe contrast sensitivity losses in the affected eye than bilateral deprivation amblyopia, perhaps due to interocular competition (Birch et al., 1998; Harwerth, Smith Iii, Paul, Crawford, & Von Noorden, 1991; Tytla et al., 1988). Conversely, bilateral deprivation amblyopia leads to greater impairments in integration tasks such as global motion perception than unilateral deprivation amblyopia (Ellemberg et al., 2002). Overall, therefore, deprivation may have a different effect on visual development than strabismus or anisometropia.

The loss of binocular vision in strabismic and anisometropic amblyopia involves active inhibition, or suppression, of cortical inputs from the amblyopic eye in favour of inputs from the fellow eye when both eyes are viewing (Baker, Meese, & Hess, 2008; Sireteanu & Fronius, 1981). For patients with strabismic or anisometropic amblyopia, it is possible to overcome suppression and utilize information from both eyes simultaneously if stimuli are presented at a higher contrast to the amblyopic eye than to the fellow eye (Black, Thompson, Maehara, & Hess, 2011; Ding, Klein, & Levi, 2013; Huang, Zhou, Lu, & Zhou, 2011; Li et al., 2011; Li et al., 2013a, 2013b; Mansouri, Thompson, & Hess, 2008; Narasimhan, Harrison, & Giaschi, 2012; Zhou, Huang, & Hess, 2013). We refer to this approach as contrast balancing.

A number of contrast balancing techniques have been developed that can be used to use quantify suppression in amblyopia (e.g. Ding & Sperling, 2006; Kwon, Wiecek, Dakin, & Bex, 2015). One such technique involves the use of a dichoptic global motion stimulus (Mansouri et al., 2008). The stimulus is constructed from a population of signal dots that move in a common direction and a population of noise dots that move randomly. The task is to identify the signal dot direction and the ratio of signal to noise in the stimulus is varied to manipulate task difficulty and measure a motion coherence threshold (percentage of signal dots required for a specific level of task performance). The use of this stimulus to assess binocular function involves two stages. Stage one is the measurement of the participant's global motion coherence threshold under non-dichoptic conditions. This measurement is then used to calibrate the signal to noise ratio in the second stage. In stage 2, the threshold number of signal dots is presented to the amblyopic eye at high contrast and the remaining noise dots are shown to the fellow eye with a variable contrast. Specifically, the contrast of the noise dots is gradually increased until the noise dots interfere with signal dot perception in the amblyopic eye resulting in poorer performance of the global motion task. The resulting contrast interference threshold is an estimation of the minimum interocular contrast difference required to overcome suppression and allow for the dichoptically presented dot populations to be perceived simultaneously and interact (Mansouri et al., 2008).

Stronger suppression assessed using contrast balancing is associated with greater deficits in visual acuity and stereoacutiy in adults (Li et al., 2011; Li et al., 2013a, 2013b) and children (Narasimhan et al., 2012) with strabismic or anisometropic amblyopia. Animal models have also revealed a link between suppression during early visual development and visual function loss in strabismus (Sengpiel, Jirmann, Vorobyov, & Eysel, 2006), strabismic amblyopia and anisometropic amblyopia (Bi et al., 2011; Smith Iii et al., 1997; Tao et al., 2014). Together, these data suggest that patients with anisometropic or strabismic amblyopia possess a structurally intact binocular visual system that is functionally suppressed under normal viewing conditions (Hess, Thompson, & Baker, 2014). This work has been the basis of new dichoptic treatments aimed at promoting binocular vision (Birch et al., 2015; Knox, Simmers, Gray, & Cleary, 2012; Li et al., 2013c, 2014; To et al., 2011).

Contrast balancing techniques have not previously been used to assess whether suppression limits binocular vision in patients with deprivation amblyopia. However, a subset of patients with deprivation amblyopia caused by unilateral or bilateral cataracts can perceive stereoscopic depth cues (Hartmann et al., 2015; Hwang, Matsumoto, & Borchert, 1999; Ing, 2011), and this is facilitated by compensating for strabismus and poor acuity (Tytla, Lewis, Maurer, & Brent, 1993). Work in this area is important because if patients with deprivation amblyopia do retain a structurally intact binocular visual system, binocular treatment approaches that have been proposed for patients with anisometropic and strabismic amblyopia (Birch et al., 2015; Eastgate et al., 2006; Hess, Mansouri, & Thompson, 2010; Hess, Mansouri, & Thompson, 2011; Hess et al., 2014; Knox et al., 2012; Li et al., 2013, 2015c, 2014; Mansouri, Singh, Globa, & Pearson, 2014; Ooi, Su, Natale, & He, 2013; Spiegel et al., 2013; To et al., 2011; Vedamurthy et al., 2015) may be indicated for patients with deprivation amblyopia.

This study aimed to assess the whether interocular suppression could be measured using contrast balancing techniques in children with unilateral or bilateral deprivation amblyopia as a first step towards investigating the use of dichoptic treatments in these patients. We determined contrast interference thresholds in children with early unilateral, early bilateral or developmental unilateral deprivation amblyopia, as well as children with anisometropic and mixed strabismus and anisometropic amblyopia. Acuity, contrast sensitivity, and global motion thresholds were also measured and compared between the groups.

2. Methods

2.1. Participants

Forty-five children (5–16 years old) were recruited through two tertiary ophthalmic centres; one in Auckland, New Zealand and one in Guangzhou, China. Human ethics committees at each site approved the study protocols, and all procedures followed the tenets of the Declaration of Helsinki. Written informed consent was obtained from parents after full explanation of the study, and assent obtained from children when appropriate. 21 children with deprivation amblyopia due to childhood cataract, 14 with anisometropic amblyopia (AA) or mixed anisometropic and strabismic amblyopia (A/S) and 10 visually normal controls were recruited (Table 1). Control children had visual acuity in each eye of 0.0 logarithm of the minimal angle of resolution in arcmin (LogMAR) or better and stereoacuity of 60 s of arc or better. Children with unilateral amblyopia had an interocular acuity difference of 0.2