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Dichoptic training improves contrast sensitivity in adults with amblyopia

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ABSTRACT

Dichoptic training is designed to promote binocular vision in patients with amblyopia. Initial studies have found that the training effects transfer to both binocular (stereopsis) and monocular (recognition acuity) visual functions. The aim of this study was to assess whether dichoptic training effects also transfer to contrast sensitivity (CS) in adults with amblyopia. We analyzed CS data from 30 adults who had taken part in one of two previous dichoptic training studies and assessed whether the changes in CS exceeded the 95% confidence intervals for change based on test–retest data from a separate group of observers with amblyopia. CS was measured using Gabor patches (0.5, 3 and 10 cpd) before and after 10 days of dichoptic training. Training was delivered using a dichoptic video game viewed through video goggles ($n = 15$) or on an iPod touch equipped with a lenticular overlay screen ($n = 15$). In the iPod touch study, training was combined with anodal transcranial direct current stimulation of the visual cortex. We found that dichoptic training significantly improved CS across all spatial frequencies tested for both groups. These results suggest that dichoptic training modifies the sensitivity of the neural systems that underpin monocular CS.

1. Introduction

For many years amblyopia was thought to be untreatable in older children and adults who were past the critical period of visual cortex development (Epelbaum et al., 1993). However, it is now evident that visual function can improve in adults with amblyopia. The gold-standard amblyopia treatment for children consists of optical correction followed by occlusion therapy (Holmes & Clarke, 2006) and there is evidence that similar approaches can also improve visual acuity in at least a subset of older children and adults with amblyopia (Kupfer, 1957; Scheiman et al., 2005; Simmers & Gray, 1999; Wick et al., 1992). These effects seem to be particularly reliable when occlusion of the fellow eye is combined with visual perceptual learning paradigms. Perceptual learning refers to an improvement in the performance of a psychophysical task after training on the task. Perceptual learning has been found to improve a range of visual functions in adults with amblyopia including Vernier acuity (Levi, Polat, & Hu, 1997) and contrast detection (Huang, Zhou, & Lu, 2008; Polat et al., 2004) (for recent reviews see Astle, Webb, & McGraw, 2011b; Levi & Li, 2009b). Perceptual learning promotes plasticity within the amblyopic visual system and the typical approach of conducting the training in a supervised laboratory setting ensures compliance with fellow eye occlusion, which can be challenging for adults.

Perceptual learning can also improve visual task performance in observers with normal vision (Epstein, 1967; Gibson, 1969, 1991). These improvements are often specific to the trained stimulus with only limited transfer of learning to other stimuli and tasks (Ball & Sekuler, 1982, 1987; Fiorentini & Berardi, 1980). However, considerable transfer of perceptual learning to other visual abilities can occur in adults with amblyopia (Levi & Li, 2009a). For example, perceptual learning of a contrast detection task at a fixed spatial

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frequency transferred to a broader range of adjacent spatial frequencies for adults with amblyopia than for controls (Huang et al., 2008). Furthermore, a variety of studies have found that monocular training on specific tasks such as Vernier acuity (Levi et al., 1997) or contrast detection (Huang et al., 2008; Polat et al., 2004) transfers to recognition acuity in adults with amblyopia. Similar effects have been achieved by combining occlusion with other visual activities such as playing video games (Li, Ngo, et al., 2011). In some cases, monocular training can also transfer to stereoacuity (Astle, McGraw, & Webb, 2011a; Li & Levi, 2004; Li, Ngo, et al., 2011).

An alternative approach to treating amblyopia that focuses on improving binocular vision has recently been proposed (Hess, Mansouri, & Thompson, 2011; Hess & Thompson, 2013). This approach, referred to here as dichoptic training, does not employ monocular occlusion. Instead, high contrast stimuli are presented to the amblyopic eye and lower contrast stimuli are presented to fellow eye in order to balance the input from the two eyes and enable binocular integration (in clinical terms this can be thought of as overcoming suppression of the amblyopic eye) (Mansouri, Thompson, & Hess, 2008). The approach is based on the hypothesis that patients with amblyopia possess an intact binocular visual system, which is rendered functionally monocular by an imbalance in the inputs from the two eyes (clinically thought of as suppression). Evidence supporting this hypothesis originates from animal models and human psychophysics. Animal neurophysiology has shown that a stronger imbalance of information between the two eyes is correlated with deeper amblyopia (Bi et al., 2011) and that antagonizing inhibitory GABA-A receptors can enhance the binocular responses of cells in the striate cortex of cats with an experimentally induced strabismus (Sengpiel et al., 2006). Comparable results have been found in humans; a larger imbalance between the two eyes (suppression) is associated with poorer visual acuity in adults and children with amblyopia (Kwon et al., 2014; Li et al., 2013a, 2013b; Li, Thompson, Lam, et al., 2011; Narasimhan, Harrison, & Giaschi, 2012) and preliminary evidence suggests that larger imbalances may also be associated with poorer outcomes following occlusion therapy (Li et al., 2013b; Narasimhan, Harrison, & Giaschi, 2012). In addition, non-invasive brain stimulation of the visual cortex, which is thought to alter neural inhibition (Fitzgerald, Fountain, & Daskalakis, 2006; Spiegel et al., 2012; Stagg et al., 2009), can improve contrast sensitivity in adults with amblyopia (Clavagnier, Thompson, & Hess, 2013; Spiegel, Byblow, et al., 2013; Thompson et al., 2008).

Initial studies have demonstrated that dichoptic training can lead to significant improvements in stereopsis and acuity without the need for occlusion of the amblyopic eye (Birch, 2013; Black et al., 2012; Hess, Mansouri, & Thompson, 2010a, 2010b; Hess et al., 2012; Knox et al., 2011; Li, Thompson, et al., 2013; Li et al., 2014; Spiegel, Li, et al., 2013; To et al., 2011). The first studies of dichoptic training used dichoptic random dot kinematograms as training stimuli whereby signal dots were presented to one eye and noise dots to the other (Hess, Mansouri, & Thompson, 2010a, 2010b). In order to make the training more engaging, more recent studies have used modified video games (Knox et al., 2011; Li, Thompson, et al., 2013; Li et al., 2014; To et al., 2011). One of these games requires the tessellation of falling blocks. Some blocks are presented to the amblyopic eye at high contrast and others are presented to the fellow eye at low contrast. Training using this approach results in patients being able to play the game with progressively less interocular contrast difference reflecting a stronger contribution of the amblyopic eye to binocular vision. Importantly, this improvement in binocular combination transfers to improved stereopsis and amblyopic eye visual acuity. The transfer of dichoptic training to monocular acuity is surprising because the dichoptic training does not involve occlusion of the fellow eye. This pattern of transfer raises the possibility that binocular imbalance plays a role in both the binocular and monocular losses that occur in amblyopia and also suggests that rebalancing the two eyes may enable plasticity within the amblyopic visual cortex (Li, Thompson, et al., 2013).

The aim of this study was to further investigate the transfer of dichoptic training to monocular visual function by assessing amblyopic eye contrast sensitivity before and after training. There are a number of reasons why it is important to know whether contrast sensitivity is improved by rebalancing the eyes and restoring binocular vision. The first is that impaired contrast sensitivity, particularly for high spatial frequencies, is a fundamental component of amblyopia (Bradley & Freeman, 1981; Hess & Howell, 1977; Levi & Harwerth, 1977) that is thought to reflect reduced responses from striate cortex neurons corresponding to the fovea (Kiorpes et al., 1998; Kiorpes & McKee, 1999). Therefore improved contrast sensitivity after treatment would implicate changes at the level of the striate cortex. Secondly, patients with amblyopia also report spatial distortions (Hess, Campbell, & Greenhalgh, 1978) that are thought to underlie the differences between grating and letter acuity in this condition. Improved letter acuity that has already been reported as a consequence of binocular treatment could reflect reduced spatial distortions rather than a direct improvement in sensitivity and spatial resolution. On the other hand, contrast sensitivity measurements are not contaminated by distortions (Hess et al., 1978), therefore an improvement in contrast sensitivity would be consistent with a specific improvement in sensitivity.

We analyzed contrast sensitivity data collected as part of two previous studies of dichoptic training for which stereopsis and visual acuity outcomes have been published (Li, Thompson, et al., 2013; Spiegel, Li, et al., 2013). Both studies found significant improvements in visual acuity and stereopsis after 10 days of training (5 days per week over 2 weeks) using the falling blocks videogame. Li, Thompson, et al. (2013) compared dichoptic training to monocular training and found that dichoptic training resulted in significantly greater improvements in visual function. Spiegel, Li, et al. (2013) found that visual cortex anodal transcranial direct current stimulation (a-tDCS) enhanced dichoptic training induced improvements in stereopsis. tDCS is a non-invasive technique for stimulating the human brain (Nitsche & Paulus, 2000). Magnetic resonance spectroscopy studies have found that a-tDCS of the human motor cortex reduces the concentration of GABA within the stimulated region (Kim et al., 2014; Stagg et al., 2009). This indicates that a-tDCS may temporarily reduce inhibitory/suppressive interactions within specific brain areas. Results from combined psychophysics and tDCS studies on participants with normal vision (Spiegel et al., 2012) and observers with amblyopia (Spiegel, Byblow, et al., 2013) suggest that a-tDCS may have a similar effect when delivered to the visual cortex. This previous work provided the motivation for testing whether combining dichoptic training with a-tDCS would lead to greater improvements than dichoptic training alone. The results showed that a-tDCS potentiated the effect of dichoptic training on stereopsis but not on acuity (Spiegel, Li, et al., 2013). Our new analysis of previously unpublished data collected during these two dichoptic training studies revealed that dichoptic training improved amblyopic eye contrast sensitivity in the majority of participants.

2. Methods

2.1. Participants

Thirty adults with amblyopia (mean age 22.2 ± 3.5 years SD) were recruited from the ophthalmology clinic at Zhongshan Ophthalmic Center, Guangzhou, China. Amblyopia was defined as