Vision Research 49 (2009) 2535–2549

Contents lists available at ScienceDirect

Vision Research

journal homepage: www.elsevier.com/locate/visres

Minireview

Perceptual learning as a potential treatment for amblyopia: A mini-review

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ARTICLE INFO

Article history:
Received 23 December 2008
Received in revised form 12 February 2009

Keywords:
Amblyopia
Perceptual learning
Sensitive period
Critical period
Internal noise
Template-retuning
Occlusion

ABSTRACT

Amblyopia is a developmental abnormality that results from physiological alterations in the visual cortex and impairs form vision. It is a consequence of abnormal binocular visual experience during the "sensitive period" early in life. While amblyopia can often be reversed when treated early, conventional treatment is generally not undertaken in older children and adults. A number of studies over the last twelve years or so suggest that Perceptual Learning (PL) may provide an important new method for treating amblyopia.

The aim of this mini-review is to provide a critical review and "meta-analysis" of perceptual learning in adults and children with amblyopia, with a view to extracting principles that might make PL more effective and efficient. Specifically we evaluate:

1). What factors influence the outcome of perceptual learning?
2). Specificity and generalization – two sides of the coin.
3). Do the improvements last?
4). How does PL improve visual function?
5). Should PL be part of the treatment armamentarium?

A review of the extant studies makes it clear that practicing a visual task results in a long-lasting improvement in performance in an amblyopic eye. The improvement is generally strongest for the trained eye, task, stimulus and orientation, but appears to have a broader spatial frequency bandwidth than in normal vision. Importantly, practicing on a variety of different tasks and stimuli seems to transfer to improved visual acuity. Perceptual learning operates via a reduction of internal neural noise and/or through more efficient use of the stimulus information by retuning the weighting of the information. The success of PL raises the question of whether it should become a standard part of the armamentarium for the clinical treatment of amblyopia, and suggests several important principles for effective perceptual learning in amblyopia.

1. Introduction

Amblyopia (from the Greek, amblyos – blunt; opia – vision) is a developmental abnormality that results from physiological alterations in the visual cortex and impairs form vision. It is a consequence of abnormal binocular visual experience during the "sensitive period" early in life.

Amblyopia is clinically important because, aside from refractive error, it is the most frequent cause of vision loss in infants and young children, occurring naturally in about 2–4% of the population; and it is of basic interest because it reflects the neural impairment which can occur when normal visual development is disrupted. The damage produced by amblyopia is generally expressed in the clinical setting as a loss of visual acuity in an apparently healthy eye, despite appropriate optical correction; however, there is a great deal of evidence showing that amblyopia results in a broad range of neural, perceptual, and clinical abnormalities (see Kiorpes, 2006; Levi, 2006 for recent reviews). Currently there is no positive diagnostic test for amblyopia. Instead, amblyopia is diagnosed by exclusion: in patients with conditions such as strabismus and anisometropia, a diagnosis of amblyopia is made through exclusion of uncorrected refractive error and underlying ocular pathology. Amblyopic patients (especially those with strabismic amblyopia) often exhibit crowding problems (Levi, 2008), meaning they have better visual acuity when letters are presented in isolation than when they are presented in a line or a full chart. Clinically, crowding is a useful sign to aid in the diagnosis of amblyopia.

Amblyopia is a significant public health problem. However, it can be reversed or eliminated when diagnosed and treated early in life. Thus, there is a premium on early detection of amblyopia and its risk factors. It has been estimated that perhaps as many as three quarters of a million preschoolers are at risk for amblyopia

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doi:10.1016/j.visres.2009.02.010

in the United States, and roughly half of those may not be detected before school age (Wu & Hunter, 2006). Improved vision screening and access to effective treatment could, in principle, substantially reduce amblyopia as a public health issue.

While amblyopia can often be reversed when treated early, conventional treatment (patching) is generally not undertaken in older children and adults. Moreover, patching itself may lead to a reduction in binocular vision and stereopsis, and to psychosocial problems such as a loss of self-esteem (Webber, Wood, Gole, & Brown, 2008). Thus, it is desirable to minimize the duration and extent of patching. A number of studies over the last twelve years or so suggest that Perceptual Learning (PL) may provide an important new method for treating amblyopia (Table 1).

Eleanor Gibson (1963) defined Perceptual Learning as "Any relatively permanent and consistent change in the perception of a stimulus array following practice or experience with this array...". Over the last half-century or so, Perceptual Learning has been studied intensively. It has formed the basis of thousands of articles, chapters and books (a Google search results in about 274,000 hits), and for this Special Issue of *Vision Research*. Indeed, advertising for the book Perceptual Learning (Fahle & Poggio, 2002; http://cognet.mit.edu/library/books/view?isbn=0262062216) states: "A familiar example is the treatment for a "lazy" or crossed eye. Covering the good eye causes gradual improvement in the weaker eye's cortical representations. If the good eye is patched too long, however, it learns to see less acutely." The focus of this review is on a rather narrower definition of perceptual learning – specifically, the notion that practicing visual tasks can lead to dramatic and long-lasting improvements in performing them, i.e., practice makes perfect! Indeed, one strong appeal of the PL approach for treating amblyopia is the widely held notion that perceptual learning can lead to permanent changes in both performance and in neural processing at an early stage of visual coding, perhaps as early as V1 (to be addressed in Sections 3 and 5). The extant evidence suggests that the primary neural damage in the amblyopic visual system takes place in the visual cortex (Kiorpes, 2006; Levi, 2006).

The aim of this mini-review is to provide a critical review of PL in adults and children with amblyopia with a view to extracting principles that might make PL more effective and efficient. Specifically we evaluate:

(1) What factors influence the outcome of perceptual learning?
(2) Specificity and generalization – two sides of the coin.
(3) Do the improvements last?
(4) How does PL improve visual function?
(5) Should PL be part of the treatment armamentarium?

Since visual acuity is the sine qua non of amblyopia, we consider not only the effect of perceptual learning on the task that is trained, but wherever possible, on Snellen acuity (see Table 1 and Figs. 1–3).

2. What factors influence the outcome of perceptual learning?

Adults are capable of improving performance on sensory tasks through repeated practice or perceptual learning (for recent reviews see Fahle, 2005; Fine & Jacobs, 2002), and this learning is considered to be a form of neural plasticity that also has consequences in the cortex (Buonomano & Merzenich, 1998). Specifically, in adults with normal vision, practice can improve performance on a variety of visual tasks, and this learning can be quite specific (to the trained task, orientation, eye, etc. – see Fahle, 2005). Interestingly, similar neural plasticity exists in the visual system of adults with naturally occurring amblyopia due to high levels of astigmatism, anisometropia, strabismus and/or form-deprivation, suggesting that perceptual learning may be a very useful approach for amblyopia treatment. Table 1 lists all (14) of the studies of PL in amblyopia published to date. These studies cover a range of tasks including Vernier acuity, contrast detection, letter identification (both first and second-order) and position discrimination. Most of the almost 200 amblyopic observers showed improvement in the trained task (7th column), although the amount of improvement varied substantially both between tasks and between individuals. This section explores the source of the considerable variance.

The effect of PL is often quantified by comparing performance before and after training, and expressed variously as a percent improvement, an improvement factor or as a ratio of threshold performance (PPR – or Post:Pre Ratio). For consistency and to simplify comparisons across studies, the effects of PL are specified as PPR in Table 1, and, where available, the number of observers showing significant learning is also provided (this information is critically important but often not provided). The PPR values for the trained task (Table 1) vary from ≈0.16 (a whopping factor of 6), to ≈0.8 (a factor of 1.2). Note that a PPR = 1 indicates no improvement, and the lower the PPR, the greater the improvement. The gray boxes in Table 1 highlight the studies where the improvement on the trained task was, on average, a factor of two or more (PPR equal to or less than 0.5). What factors distinguish studies in which learning is small from those in which learning is substantial?

2.1. Age

Because amblyopia only occurs when there is abnormal binocular visual input during the "sensitive period" early in life, it is often assumed that it can only be treated effectively in infants and young children. The studies listed in Table 1 span a broad range of ages – from 7 to 60 years, all outside the conventional sensitive period that is thought to extend to about six. Does age matter?

We suspect that age does not account for the variance across studies. For example, a number of studies with only adults (18 and over) show strong learning (e.g. Levi & Polat, 1996; Li, Klein, & Levi, 2008) while some with only children (e.g. Li, Young, Hoenig, & Levi, 2005) show relatively weak learning. Moreover, neither Polat, Ma-Naim, Belkin, and Sagi (2004) nor Chen, Chen, Fu, Chien, and Lu (2008) found any correlation between age and outcome in their subject populations. Fig. 1 summarizes graphically the effect of age on both the trained task (top panel) and transfer to Snellen acuity (Lower panel). The regression lines (dashed) show a very weak dependence on age in opposite directions in the two panels ($r = 0.20$ for the trained task and -0.25 for Snellen). Note that we have not included the Fronious data (Fronius, Cirina, Cordey, & Ohrloff, 2005; Fronius, Cirina, Kuhli, Cordey, & Ohrloff, 2006) in the regression, because it is not possible to distinguish between the role of perceptual learning and the loss of the fellow eye, in improving performance. Inspection of Fig. 1 suggests that age, at least within the post sensitive-period years from ≈10 to 40, has little influence on the outcome of PL.

2.2. Task

Fig. 2 compares the effects of PL across tasks (trained task – top; Snellen acuity – bottom). Here it is instructive to compare the tasks that result in the most improvement (lowest PPR values) and those that result in the least (highest PPR values). For the trained task (Fig. 2 top panel), five studies result in PPR values below 0.4 (i.e., a factor of 2.5 or more improvement). Four of the five involve repeated measurements of contrast sensitivity. One (Polat et al., 2004 – green diamond) used high contrast flankers at different separations from the target, to train "lateral interactions". Both