Vision Research 114 (2015) 4–16

Contents lists available at ScienceDirect

Vision Research

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

Amblyopia and the binocular approach to its therapy

Robert F. Hess [a,*], Benjamin Thompson [b,c]

[a] McGill Vision Research, McGill University, Montreal, Canada
[b] Department of Optometry and Vision Science, University of Waterloo, Canada
[c] Department of Optometry and Vision Science, University of Auckland, New Zealand

ARTICLE INFO

Article history:
Received 4 November 2014
Received in revised form 9 February 2015
Available online 20 April 2015

Keywords:
Amblyopia
Suppression
Binocular therapy
Metaplasticity

ABSTRACT

There is growing evidence that abnormal binocular interactions play a key role in amblyopia. In particular, stronger suppression of the amblyopic eye has been associated with poorer amblyopic eye visual acuity and a new therapy has been described that directly targets binocular function and has been found to improve both monocular and binocular vision in adults and children with amblyopia. Furthermore, non-invasive brain stimulation techniques that alter excitation and inhibition within the visual cortex have been shown to improve vision in the amblyopic eye. The aim of this review is to summarize this previous work and interpret the therapeutic effects of binocular therapy and non-invasive brain stimulation in the context of three potential neural mechanisms; active inhibition of signals from the amblyopic eye, attenuation of information from the amblyopic eye and metaplasticity of synaptic long term potentiation and long term depression.

1. Introduction

Amblyopia therapy is a large area as many different treatments have been proposed over the last 100 years. One promising approach for the treatment of adults with amblyopia is the combination of patching and perceptual learning in its many varied forms, for which both monocular and binocular benefits have been documented. More recently, the focus of research in this area has shifted from monocular interventions that involve patching of the fellow eye to approaches that directly target binocular visual function and as the primary therapeutic step. The emerging field of binocular approaches to amblyopia therapy is the topic of this review.

It is accepted that abnormal binocular visual experience in early childhood causes amblyopia and that suppression (typically measured using the worth 4 dot test) plays an important part of the clinical diagnostic picture. It has also been shown that loss of binocularity is one of the defining features of amblyopia (McKee, Levi, & Movshon, 2003) However the potential importance of binocular approaches to amblyopia therapy has only recently received widespread attention (Birch et al., 2014; Cleary et al., 2009; Hess, Mansouri, & Thompson, 2010; Hess, Thompson, & Baker, 2014; Hess et al., 2014; Li, Thompson, et al., 2013; Li et al., 2014; Mansouri et al., 2014; Ooiemail, Su, Natale, & He, 2013; Spiegel, Li, et al., 2013; To et al., 2011). This has led to increased interest in the development of amblyopia treatments that directly address binocular dysfunction by promoting binocular vision and reducing inhibitory interactions within the visual cortex. In this review, we first summarize emerging approaches to the treatment of amblyopia that emphasize binocular visual function. We then describe the relationship between suppression of the amblyopic eye and the depth of amblyopia and explore whether suppression is due to active inhibition of information from the amblyopic eye or is simply the result of attenuated amblyopic eye signals. The concept of metaplasticity is then introduced and applied to the recovery of visual function in amblyopia. Finally, the results of studies into the application of non-invasive visual cortex stimulation to amblyopia are summarized and placed in the context of inhibition, attenuation and metaplasticity.

2. Emerging treatment options for amblyopia

Patching therapy has been used to treat amblyopia for hundreds of years even though its shortcomings are many; compliance is poor (Searle et al., 2002) because of the social and psychological difficulty of forcing a child to wear a patch combined with the impaired vision experienced by the child when the patch is in place (Holmes et al., 2003; Webber et al., 2008). Although 79% of children show at least a 2 line improvement after 4 months of patching (Repka et al., 2003), 25% of these children will regress to some degree once the patch is removed (Holmes et al., 2004). More

* Corresponding author.
E-mail address: robert.hess@mcgill.ca (R.F. Hess).

http://dx.doi.org/10.1016/j.visres.2015.02.009
0042-6989/

importantly, the binocular outcome is often poor regardless of the improved amblyopic eye acuity (Birch, 2012). One reason for this is likely to be the nature of the viewing conditions during patching (i.e. monocular) compared with those after patching, namely binocular viewing. We do not yet know how patching works, although possible mechanisms include a reduction of interocular suppression or a purely monocular improvement in the processing of signals from the amblyopic eye. Since there is such a poor binocular outcome from patching, it may be safe to conclude that the effects of patching primarily involve monocular mechanisms.

There have been a number of suggestions for improving the therapeutic approach to amblyopia. Some of these are purely monocular, some are monocular under otherwise binocular conditions and one is purely binocular, involving dichoptic stimulation and a dichoptic manipulation of contrast to enable simultaneous use of both eyes. A summary of different treatment suggestions is shown in Fig. 1. The first attempt to provide the combination of short-term occlusion (20 min), controlled visual stimulation and attentive game play (noughts and crosses) was the CAM treatment (Campbell et al., 1978). Its beneficial effects were later isolated to the short term nature of the occlusion and the attentive game play (Mitchell, Howell, & Keith, 1983). Another step in terms of the monocular approach was Neurovision in which perceptual learning for threshold detection was combined with short-term patching (Bonneh, Sagi, & Polat, 2004; Polat et al., 2004, 2005). There is no doubt that perceptual

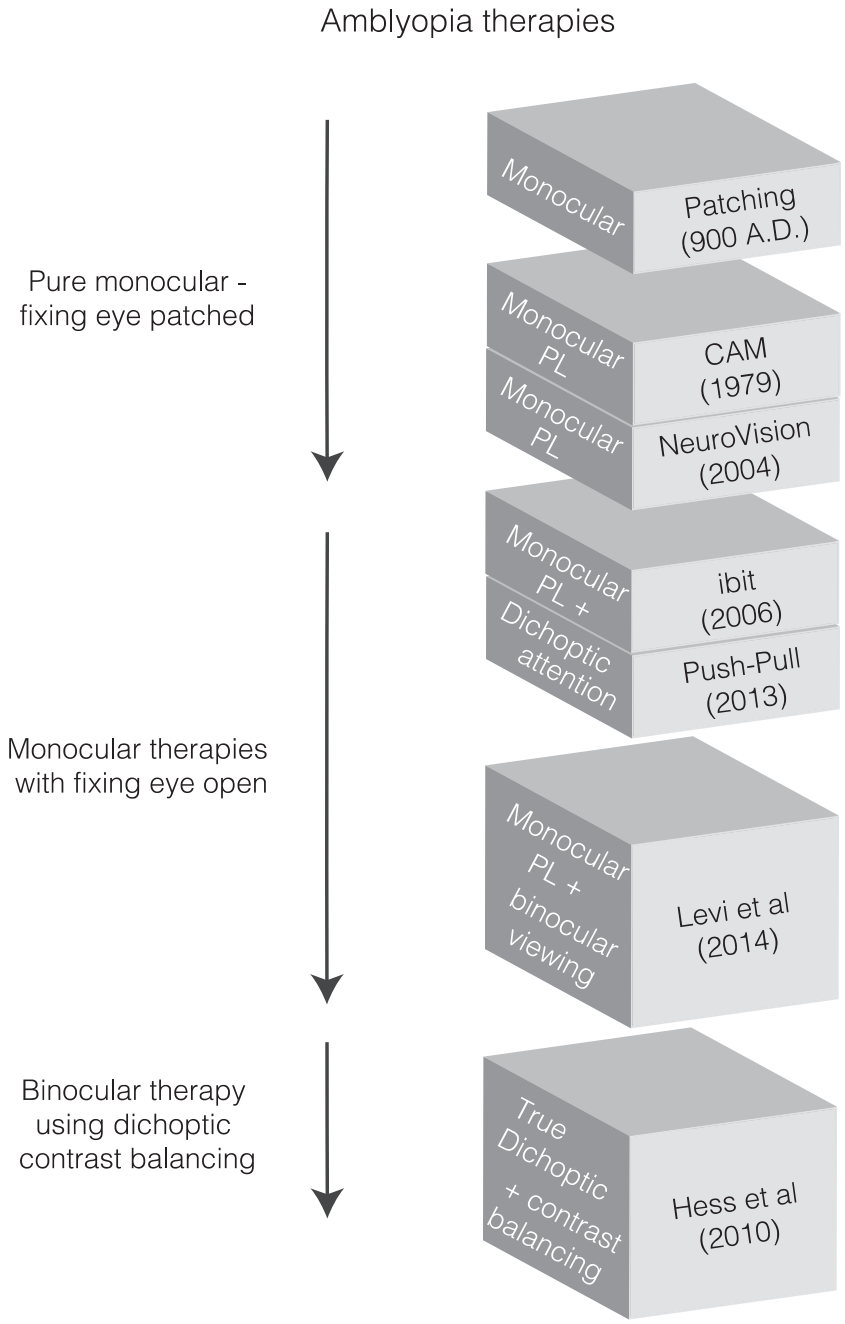

Fig. 1. A summary of different principled approaches to the treatment of amblyopia, some purely monocular, some containing a binocular element and others purely binocular with dichoptic manipulation of parameters. Because the literature on monocular perceptual learning is large, only representative examples are shown. Also, there are a number of behavioral optometric approaches (Press, 1981) that are not included as these are beyond the scope of this review.