Available online at www.sciencedirect.com
SCIENCE DIRECT®
Vision Research 45 (2005) 2810–2819
Vision Research
www.elsevier.com/locate/visres

Spatial interactions reveal inhibitory cortical networks in human amblyopia

Erwin H. Wong [a,*], Dennis M. Levi [a,b], Paul V. McGraw [c]

[a] School of Optometry, University of California, Berkeley, CA 94720, USA
[b] Helen Wills Neuroscience Institute, University of California, Berkeley, CA 94720, USA
[c] Department of Optometry, University of Bradford, Bradford BD7 1DP, UK

Received 24 August 2004; received in revised form 1 June 2005

Abstract

Humans with amblyopia have a well-documented loss of sensitivity for first-order, or luminance defined, visual information. Recent studies show that they also display a specific loss of sensitivity for second-order, or contrast defined, visual information; a type of image structure encoded by neurons found predominantly in visual area A18/V2. In the present study, we investigate whether amblyopia disrupts the normal architecture of spatial interactions in V2 by determining the contrast detection threshold of a second-order target in the presence of second-order flanking stimuli. Adjacent flanks facilitated second-order detectability in normal observers. However, in marked contrast, they suppressed detection in each eye of the majority of amblyopic observers. Furthermore, strabismic observers with no loss of visual acuity show a similar pattern of detection suppression. We speculate that amblyopia results in predominantly inhibitory cortical interactions between second-order neurons.

Keywords: Amblyopia; Second-order; Lateral interactions; Visual cortex

1. Introduction

Amblyopia is a disorder of spatial vision, usually present in one eye, which results from discordant binocular input to the visual cortex during development. Amblyopia is typically associated with strabismus (eye misalignment) or anisometropia (unequal refractive error). A loss of contrast sensitivity for first-order (luminance defined) spatial information is well documented in amblyopic eyes, and is widely attributed to neural deficits at the level of striate cortex (V1) (Kiorpes & McKee, 1999). Neurophysiological studies have shown that the response of V1 neurons to a first-order, near threshold stimulus placed within its receptive field can be facilitated (response increased) (Bakin, Nakayama, & Gilbert, 2000; Kapadia, Ito, Gilbert, & Westheimer, 1995; Nelson & Frost, 1985; Polat, Mizobe, Pettet, Kasamatsu, & Norcia, 1998) or suppressed (response reduced) (Knierman & Van Essen, 1992; Levitt & Lund, 1997; Walker, Ohzawa, & Freeman, 1999) by flanking first-order stimuli. The type of interaction, i.e., facilitatory or suppressive, depends upon the spatial distance between target and flanks, the relative orientation difference between the elements that comprise the target and flanks, and the magnitude of the flank contrast (Kapadia, Westheimer, & Gilbert, 1999; Polat et al., 1998). Such cortical interactions are thought to form the cellular basis to psychophysical demonstrations of enhanced visibility for first-order stimuli flanked by facilitatory masks. Psychophysical studies have shown that target and flank conditions which produce facilitation (lower the contrast detection threshold) in normal eyes (Kapadia et al., 1995; Levi, Hariharan, & Klein, 2002; Polat & Sagi, 1993, 1994; Yu, Klein, & Levi,

* Corresponding author. Tel.: +1 314 516 6516; fax: +1 314 516 5150.
E-mail addresses: wonge@umsl.edu (E.H. Wong), dlevi@berkeley.edu (D.M. Levi), p.v.mcgraw@bradford.ac.uk (P.V. McGraw).

0042-6989/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.visres.2005.06.008

2002) can result in suppression (increase the contrast detection threshold), or reduced facilitation, in amblyopic eyes (Levi et al., 2002; Polat, Sagi, & Norcia, 1997). However, Polat, Ma-Naim, Belkin, and Sagi (2004, 2005) has reported reduced facilitation in amblyopic eyes only for high spatial frequency stimuli, and in strabismic amblyopes more than anisometropic amblyopes.

Neurophysiological studies have shown that the transition from facilitatory to suppressive interactions reflects the spatial distribution of target and flanks either within the classic receptive field (CRF) or its inhibitory surround. The excitatory CRF and larger ($\geqslant 2\times$) overlapping inhibitory region form a center-surround mechanism (Angelucci et al., 2002; Cavanaugh, Bair, & Movshon, 2002a, 2002b) in which stimulation of the annular surround suppresses the CRF response through divisive modulation of the response gain but can not drive the CRF directly (Cavanaugh et al., 2002a, 2002b). Anatomical evidence indicates that the excitatory spatial limit of the CRF is formed by horizontal connections within V1 (i.e., connections between cortical columns) and the inhibitory surround is largely formed by feedback connections from V2 to V1 (Angelucci et al., 2002; Cavanaugh et al., 2002a; but see Stettler, Das, Bennett, & Gilbert, 2002). Therefore, the abnormal pattern of spatial interactions for first-order visual stimuli reported in amblyopic observers could result from either abnormal horizontal connections in V1, and/or feedback connections from V2 to V1.

In comparison with the striate cortex, much less is known about the effects of amblyopia on extra-striate cortical structure and function. Visual processing in the extra-striate cortex (V2) can be investigated using second-order spatial stimuli, e.g., a visual stimulus defined by contrast modulations. Contrast modulation frequencies are not represented in the Fourier spectrum of an image, and therefore demodulation is required for stimulus detection—this has been extensively modeled as a filter-rectify-filter processing cascade (Chubb & Sperling, 1988). Briefly, luminance modulations of high spatial frequencies undergo linear filtering in V1, the output is rectified (the demodulation step), and this enables contrast modulations of low spatial frequencies to be detected by a second-stage of linear filtering. There is compelling psychophysical evidence that first-order and second-order spatial information can be processed independently in the visual cortex (Schofield & Georgeson, 1999, 2003; Willis, Smallman, & Harris, 2000). Furthermore, physiological studies in cat (Mareschal & Baker, 1998; Zhou & Baker, 1994) and monkey (Leventhal, Wang, Schmolesky, & Zhou, 1998; von der Heydt & Peterhans, 1984, 1989) place the locus of the second filtering stage predominantly in area 18/V2.

In a previous study, we demonstrated a specific loss of second-order sensitivity in individuals with amblyopia (Wong, Levi, & McGraw, 2001). However, it is presently unknown whether the pattern of spatial interactions which occur in the visual cortex of normal, or amblyopic observers, are qualitatively or quantitatively similar for first- and second-order stimuli. We examine this issue by psychophysically determining contrast detection threshold for a second-order target in the presence of collinear or orthogonal second-order flanks (equated for visibility) in normal observers (control), amblyopic observers, and observers with strabismus but no loss of visual acuity. We found the flanking effect to be facilitative in normals but suppressive in each eye of most amblyopic and strabismic observers (subsequently referred to as non-control observers). We speculate that human amblyopia results in predominantly inhibitory horizontal interactions between second-order neurons.

2. Methods

2.1. Observers

Six amblyopic observers, two observers with strabismus but no loss of visual acuity, and five normal (control) observers participated in the experiment. All observers were adults and the visual characteristics of the non-control observers are presented Tables 1A and B. Control observers had normal or corrected-to-normal vision. All observers were highly practiced at making psychophysical judgements, wore refractive correction as required, and all but the author (EW) were naïve to the task. Informed consent following the guidelines of either the University of Houston or the University of California was obtained from all observers prior to data collection.

2.2. Apparatus

Stimuli were generated using the macro capabilities of NIH Image 1.62f (available from http://rsb.info.nih.gov/nih-image/). The host computer was an Apple Power Macintosh 6500/225 and stimuli were presented on a Dell monitor (21-inch screen, resolution 1024×768 pixels, frame refresh rate 75 Hz, and mean luminance 15 cd/m^2). The monitor output was made linear over the entire range used in the experiment via calibration with a photometer (Minolta LS-110 digital luminance meter). To obtain accurate control of luminance contrast we increased the number of intensity levels from 8 to 12 bits by combining the outputs of the red, green, and blue guns via a video summation device (Pelli & Zhang, 1991).

2.3. Stimuli

We used stationary, contrast modulations of random static noise as second-order stimuli (Fig. 1). Stimuli were