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Latent binocular function in amblyopia

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ABSTRACT

Recently, psychophysical studies have shown that humans with amblyopia do have binocular function that is not normally revealed due to dominant suppressive interactions under normal viewing conditions. Here we use magnetoencephalography (MEG) combined with dichoptic visual stimulation to investigate the underlying binocular function in humans with amblyopia for stimuli that, because of their temporal properties, would be expected to bypass suppressive effects and to reveal any underlying binocular function.

We recorded contrast response functions in visual cortical area V1 of amblyopes and normal observers using a steady state visually evoked responses (SSVER) protocol. We used stimuli that were frequency-tagged at 4 Hz and 6 Hz that allowed identification of the responses from each eye and were of a sufficiently high temporal frequency (>3 Hz) to bypass suppression. To characterize binocular function, we compared dichoptic masking between the two eyes in normal and amblyopic participants as well as interocular phase differences in the two groups.

We observed that the primary visual cortex responds less to the stimulation of the amblyopic eye compared to the fellow eye. The pattern of interaction in the amblyopic visual system however was not significantly different between the amblyopic and fellow eyes. However, the amblyopic suppressive interactions were lower than those observed in the binocular system of our normal observers. Furthermore, we identified an interocular processing delay of approximately 20 ms in our amblyopic group.

To conclude, when suppression is greatly reduced, such as the case with our stimulation above 3 Hz, the amblyopic visual system exhibits a lack of binocular interactions.

1. Introduction

Amblyopia is a condition in which there is profound abnormality of binocular vision. Animal studies have suggested that there is a loss of cells receiving input from both eyes and an increase in the number of cells that receive monocular input (Blakemore, Garey, & Vital-Durand, 1978; Eggers & Blakemore, 1978; Wiesel & Hubel, 1965). While initially this was thought to be structural in nature, some later studies argue for a functional basis by showing that it can be pharmacologically reversed (Mower, Christen, Burchfiel, & Duffy, 1984). Traditionally, humans with amblyopia were thought to have irretrievably lost binocular vision and so treatment has been focussed on recovery of monocular function using occlusion of the fellow good eye (P.E.D.I.G., 2005). Psychophysical studies recently have argued that amblyopes have binocular function that is latent and only revealed when the suppressive interactions that normally block the participation of the amblyopic eye are eliminated (Baker, Meese, & Hess, 2008; Baker, Meese, Mansouri, & Hess, 2007; Mansouri, Thompson, & Hess, 2008). There are new treatment approaches now that specifically involve recovery of binocular function by eliminating suppression (Kelly et al., 2016; Li et al., 2015; To et al., 2011). These approaches assume that normal binocular vision results once suppression is eliminated, so it is important to understand the nature of binocular interactions for stimuli that do not initiate strong suppression and how they relate to that of a normal binocular visual system.

A recent study (Huang, Baker, & Hess, 2012) of amblyopic suppression using temporally modulated stimuli showed that suppression of the amblyopic response, while being evident for 1 Hz stimulation, is virtually abolished by 3 Hz stimulation for a wide range of dichoptic noise stimuli (e.g. overlay, surround and combined overlay and surround masks). What this means for the present use of temporally-tagged stimuli of 4 Hz and 6 Hz is that the degree of suppression evoked by these steady-state stimuli should be minimal and comparable, making them ideal probes of the latent binocular function not normally revealed because of the overriding influence of more dominant suppression effects.

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Furthermore, we have recently shown that magnetoencephalography (MEG) combined with the frequency-tagging of left and right eye responses is an ideal way of characterizing binocular contrast interactions in normal individuals (Chadnova, Reynaud, Clavagnier, & Hess, 2016). Dichoptic contrast responses in normal observers can be modeled in terms of the binocular normalization that has been proposed from psychophysical (Ding & Sperling, 2006; Meese, Georgeson, & Baker, 2006) and fMRI (Moradi & Heeger, 2009) studies. This provided a basis against which binocular signal interactions in amblyopia can be compared. We set out to answer two questions: first, once active suppression is eliminated are the dichoptic interactions in amblyopia of a normal form? Second, if there are anomalies in dichoptic interactions beyond active suppression, can these be modelled by an input attenuation of the amblyopic eye (Baker et al., 2008), a change in gain or both?

Measuring steady-state visually evoked response (SSVER) using MEG we quantify interocular interactions as a first step towards addressing the above questions. We use temporal frequency-tagging to identify left and right eye responses to document how the contrast responses are altered under different conditions of reciprocal amblyopic/fellow eye stimulations. Using the canonical binocular normalization model (Ding & Sperling, 2006; Meese et al., 2006; Moradi & Heeger, 2009) we show that binocular combination in the amblyopic visual system is subtly different and this difference is characterized by reduced gain as well as attenuation of the input from the amblyopic eye. Furthermore, we observed a processing delay between the eyes of amblyopes compared with normal observers.

2. Methods

2.1. Participants

The work presented here consists of two protocols tested on different days: magnetoencephalography (MEG) and psychophysics. We collected MEG data from seven amblyopic participants (2 females, 5 males, age: 32 ± 11.6, see amblyopia characteristics of participants in Table 1), one of them could not participate in the psychophysics test. We used data from 4 participants from our previous experiment (4 males, mean age 32.5 ± 5.9 years) as a normal observers group (Chadnova et al., 2016). We collected additional data on these four participants for the monocular delay between their eyes as well as their psychophysical threshold.

All participants signed the informed consent form that has been approved by the Ethics Review Board of the Montreal Neurological Institute, consistent with the Declaration of Helsinki.

2.2. Stimuli and procedures

The stimuli were programmed using the Psychophysics toolbox (Brainard, 1997; Pelli, 1997) in Matlab and presented on a 60 Hz refresh rate gamma-corrected 3 D LG monitor (23″, 1920 × 1080, active area 509 × 290 mm) with a set of polarizers to provide the dichoptic stimulation. The mean gray luminance of the screen was 112 cd/m^2. The polarizers reduced the luminance of the screen to about 40% of its baseline level. The monitor was 170 cm from the observer.

We used a steady state visually evoked responses (SSVERs) paradigm (Norcia, Appelbaum, Ales, Cottereau, & Rossion, 2015). A visual stimulus consisted of a binary noise pattern presented dichoptically and projected to each eye at 4 Hz and 6 Hz, respectively (Fig. 1). We sinusoidally modulated the stimuli in an on/off mode, from the noise patterns to the mean luminance. The two eyes stimuli were overlapping on the screen but directed to each eye by means of polarized glasses. The stimulus duration was 4 s,

Table 1
Amblyopia subject characteristics.

	Age, sex	Amblyopic eye	Refraction (diopter)		Acuity		Squint	Stereo	Clinical suppression	History
			OS	OD	OS	OD				
A1	M, 54 y.o.	OS, mixed	+2	+2	20/125	20/12.5	OS, esotropia 4°	None	Strong	Detected at 3 years; no patching, no surgery
A2	M, 23 y.o.	OS, mixed	+2	−0.5	20/63	20/16	OS, exotropia 2.5°	None	mild	Detected at 15 years; no patch; no surgery
A3	M, 25 y.o.	OS, mixed	+5.25/−2.25 × 30°	+3.5	20/100	20/16	OS, exotropia 4°	None	mild	Detected at 5 years; patch for 3 months all day long; no surgery
A4	F, 25 y.o.	OD, strabismus	plano	−0.75/−0.5 × 60°	20/20	20/63	OD, exotropia 15°	None	Strong	Detected: 2 years; patch: 5 years; 2 surgeries
A5	M, 42 y.o.	OD, strabismus	−1.25/−0.25 × 103°	+0.5/−1.25 × 90°	20/12.5	20/80	OD, exotropia 10°	None	mild	Detected: 10 years; patch: 1 year + training; no surgery
A6	M, 26 y.o.	OD, strabismus	+0.5/−0.25 × 90°	+1.5	20/20	20/80	OD, exotropia1°	800 arcsec	Strong	Detected at 20 years; no patch; no surgery
A7	F, 29 y.o.	OD, mixed	−1.25	+2/−1 × 60°	−0.2	0.5	OD, exotropia 2°	800 arcsec	Strong	Detected at 10 years; patch for 6 months; no surgery