VISION

Vision Research 49 (2009) 287-294

Contents lists available at ScienceDirect



Vision Research

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

Strabismic amblyopes show a bilateral rightward bias in a line bisection task: Evidence for a visual attention deficit

Aylin Thiel^{a,b,*}, Ruxandra Sireteanu^{a,b,c}

^a Department of Biological Psychology, Institute for Psychology, Goethe University, Mertonstrasse 17, 60054 Frankfurt, Germany

^b Department of Neurophysiology, Max Planck Institute for Brain Research, Frankfurt, Germany ^c Department of Biomedical Engineering, College of Engineering, Boston University, Boston, USA

ARTICLE INFO

Article history: Received 14 January 2008 Received in revised form 19 July 2008

Keywords: Human amblyopia Line bisection Bilateral minineglect Attention

ABSTRACT

Neurologically normal observers show a consistent leftward bias when asked to bisect a horizontal line ("pseudoneglect"). In this study, we found that subjects with strabismic and strabismic-anisometropic amblyopia show a consistent rightward bias ("minineglect") in a line bisection task. The bias was seen in both eyes, but affected more strongly the amblyopic eye. Purely anisometropic amblyopes show a similar bias, affecting only the amblyopic eye. The group of strabismics with alternating fixation did not differ significantly from normal observers. These errors are reminiscent of the attentional neglect of the left extrapersonal space, shown by subjects with lesions in the right posterior parietal cortex. We suggest that an early strabismus might lead to a functional deficit of the dorsal cortical pathway, in addition to the well-known impairments on the ventral visual pathway. We conclude that strabismic amblyopes might show subtle attentional deficits, in addition to their unilateral vision loss.

© 2008 Elsevier Ltd. All rights reserved.

1. Introduction

In the neurological condition known as "hemineglect" (or simply "neglect"), patients disregard the left side of their extrapersonal space (cf. Heilman, 1979; Heilman, Watson, & Valenstein, 1985). When asked to bisect a horizontal line, they set the perceived middle too far to the right; when asked to draw a figure, their drawings usually lack the left side (Halligan & Marshall, 1992; Schenkenburg, Bradford, & Ajax, 1980). These deficits are interpreted as an impairment in the orienting of spatial attention. They are usually associated with a lesion in the right posterior parietal cortex, including the temporo-parietal junction (inferior parietal lobule: Vallar & Perani, 1986), or the superior temporal region (Karnath, Ferber, & Himmelbach, 2001; for a review, see Pisella & Mattingley, 2004).

Neurologically normal observers display a reverse asymmetry of more modest proportions, which is usually called "pseudoneglect": when asked to bisect a horizontal line, the perceived middle is set too far to the left; objects located in the left side of the extrapersonal space are perceived as larger than on the right (Bowers & Heilman, 1980; Fronius & Sireteanu, 1992; Halligan & Marshall,

* Corresponding author. Present address: Department for Psychiatry, Psychosomatics and Psychotherapy, University Hospital, Goethe University, Frankfurt, Germany. Fax: +49 69 96769 742.

E-mail address: Aylin.Thiel@kgu.de (A. Thiel).

1992; Schelchshorn, Yoo, Chung, & Sireteanu, 1998; von Helmholtz, 1896). This asymmetry occurs in children as young as 4.5 years of age (Chockron & De Agostini, 1995) and is dependent on reading habits (Chockron & Imbert, 1993). Left-handed observers show a more variable pattern of asymmetry (Bradshaw, Nettleton, Wilson, & Bradshaw, 1977; Scarisbrick, Tweedy, & Kulanski, 1987; Schelchshorn et al., 1998). A left pseudoneglect was observed in right-handed adult observers also in other modalities (tactile or kinesthetic: Bowers & Heilman, 1980; Halligan, Manning, & Marshall, 1991; auditory: Goertz & Sireteanu, submitted for publication). This supramodal overestimation of objects located in the left hemispace could be interpreted as a developmental bias towards the most attended (usually the left) side of the extrapersonal space.

Recently, we found that children with developmental dyslexia did not show the normally occurring "pseudoneglect": when asked to bisect a horizontal line, 8–12-year-old dyslexic children set the perceived middle too far to the right, thus displaying a subtle, but consistent "minineglect" (Sireteanu, Goebel, Goertz, & Wandert, 2006; Sireteanu, Goertz, Bachert, & Wandert, 2005). We interpreted these results as evidence that children with developmental dyslexia present deficits in orienting of visual attention, which occur in addition to their well-known phonological deficits (for a review, see Habib, 2000). We suggested that developmental dyslexia might be associated with a disturbance in a string of cortical areas, involving the posterior parietal cortex on both sides of the brain (Sireteanu et al., 2005).

^{0042-6989/\$ -} see front matter \odot 2008 Elsevier Ltd. All rights reserved. doi:10.1016/j.visres.2008.08.005

In the present work, we investigated whether a similar bias might occur in another neurodevelopmental disorder, namely childhood amblyopia. In this condition, disturbances occurring in early childhood, like an ocular misalignment (strabismus) or an uncorrected refractive imbalance of the two eyes (anisometropia), lead to a loss of binocular functions, which in turn can be followed either by the chronic suppression of one eye, or by the alternating suppression of each eye. The most disrupting consequences occur with constant interocular suppression. The functional losses in the chronically suppressed eye include impairments in visual acuity and contrast sensitivity, abnormal contour interaction ("crowding"), mislocalization of visual stimuli, disturbed oculomotor functions, and disrupted eye-hand coordination (for reviews, see Levi & Carkeet, 1993; McKee, Levi, & Movshon, 2003; Sireteanu, 2000). In addition, spatial and temporal misperceptions were reported (Barrett, Pacey, Bradley, Thibos, & Morill, 2003; Bäumer & Sireteanu. 2006: Bedell & Flom. 1983: Fronius & Sireteanu. 1989. 1992, 1994; Hess, Campbell, & Greenhalgh, 1978; Lagrèze & Sireteanu, 1991; Sireteanu, Bäumer, Sârbu, & Iftime, 2007; Sireteanu & Fronius, 1989; Sireteanu, Lagrèze, & Constantinescu, 1993; Sireteanu, Thiel, Fikus, & Iftime, 2008).

Several neuroimaging studies have shown that human amblyopia is associated with reduced cortical activation through the affected eye, mainly in regions on the ventral visual pathway (cf. Barnes, Hess, Dumoulin, Achtmann, & Pike, 2001; Muckli et al., 2006). Recent psychophysical studies suggest that there might be deficits also in regions on the dorsal visual pathway of strabismic amblyopes (Ho & Giaschi, 2006; Ho et al., 2006; Simmers, Ledgeway, Hess, & McGraw, 2003; Simmers, Ledgeway, Mansouri, Hutchinson, & Hess, 2006; but see Levi & Tripathy, 2006). Thus, it seems that both pathways are affected, even if to a different degree.

Here, we investigated whether adult amblyopic subjects show a rightward bias in a line bisection task. We reasoned that, if amblyopic subjects show impairments on the dorsal visual pathway (possibly involving the parietal visual cortex), they ought to show a reduced attentional bias towards the left extrapersonal space ("minineglect"). In amblyopes with a history of strabismus, this deficit should be present in both eyes.

2. Methods

2.1. Selection of the subjects, inclusion criteria

The subjects were recruited by leaflets distributed in the Frankfurt University and by word-of-mouth. They were remunerated ($10.00 \in \text{per}$ hour) for their participation (orthoptic assessment was not reimbursed). Testing was done in accordance with the tenets of the Declaration of Helsinki. Written informed consent was obtained from all subjects after the nature and purpose of the study had been fully explained. The study had been approved by the Ethics Committee of the Frankfurt University.

Criteria for inclusion in the study were: no known ocular, neurological or psychiatric abnormalities; no medication taken during the last 24 h before the experiments. Prior to the experiments, the subjects were given a complete orthoptic examination by a professional orthoptist. This examination included: corrected decimal visual acuity (visus cc) for near, measured with a test with logMAR spacings (the C-Test, Oculus, Dutenhofen) at 40 cm distance; angle of squint, assessed with the simultaneous and alternate cover and prism tests for far and near fixation; and pattern of fixation, determined with the aid of a visuscope. Stereopsis was assessed with the TNO-Test. For the evaluation of retinal correspondence, the subjects were tested with the Maddox cross in connection with dark and light red filters and with Bagolini striated glasses for far and near vision. Eye dominance for near was assessed using a cover test. To be classified as unilaterally amblyopic, the subjects had to show a difference of at least two lines on a decimal acuity chart and a visual acuity of at least 1.0 in the dominant eye. Subjects with a refraction difference of at least 1.5 D spheric equivalent were deemed anisometropic. To avoid the possible effects of handedness (Bradshaw et al., 1977; Scarisbrick et al., 1987), only righthanded subjects were included in the control group. Only one of the experimental subjects (SG) was left-handed.

The results of this study were based on data from 30 subjects: five strabismically amblyopic subjects, five strabismic and anisometropic amnlyopes, five purely anisometropic amblyopes, eight strabismics with alternating fixation and good vision in both eyes, and seven normally sighted subjects (see Table 1). The ages of the experimental subjects ranged from 20 to 61 years (15 females, 13 males; mean age 31.2 years), those of the control subjects from 20 to 63 years (4 females, 3 males; mean age 31.4 years).

2.2. Materials and procedure

All subjects were tested wearing their best possible correction. The method was adapted from McCourt (2001) and was identical to that used in our previous experiments (Sireteanu et al., 2005, 2006). The subjects were seated in front of a computer monitor, in a darkened room. The observer's head was placed on a chin-rest, in order to keep an eye-to-monitor distance of 57 cm. The subjects were asked to fixate monocularly at the center of the screen. Occlusion was performed with a monocular patch. All subjects were naïve to the purpose of the experiments.

The subjects were presented with horizontal lines of two different lengths (14.8° and 22.2°) on the computer screen. The lines could be presented for either 100 or 1000 ms. Mean luminance of the screen was 30 cd/m^2 . The lines were 0.3° high, and they were pretransected, with the two parts having different black-and-white polarities on the gray background. The luminance of the white portion of the lines was 125.3 cd/m^2 , that of the black portion 19.4 cd/m², thus yielding a Michelson contrast of 0.73 The subjects' task was to indicate, by pressing one of two keys on the computer board, which of the sides of the pretransected lines was perceived as longer. Transector location vas varied according to a weighted up-down method (Kaernbach, 1991).

According to Kaernbach (2001), step size might influence the slopes of the psychometric function obtained with an adaptive procedure. In our previous study (Sireteanu et al., 2005), the spread of the psychometric function was approximately 0.5°. Following the suggestion of Kaernbach (1991), we used 0.1° as the step size, which is nearly one sixth of this difference. In case of a correct answer, the transector was shifted 0.1° to the veridical middle; in case of an incorrect answer, the transector was shifted 0.3° away from the veridical middle. The starting point was selected such that the chance to answer correctly was over 90%. The equilibrium condition for convergence of performance was 75%.

Each trial consisted of 240 repetitions, with no other terminating condition of the weighted up-down procedure. We used four factors for each two different conditions, which were permutated over all other conditions between subjects. The different factors were: time of presentation (100 or 1000 ms), length of the line (14.8° or 22.2°), polarity of the upper part of the line (black or white), and side of transection (leftward or rightward). For each subject, the sequence of testing of the dominant and the non-dominant eye was balanced during each experimental session (ABBA or BAAB). The displacement of the transector was the independent variable, the answer the dependent variable. The psychometric functions generated from the adaptive data were calculated through logistic regression (Kaernbach, 1991). The point of subjec-

Table 1

Orthoptic data of the experimental subjects

Subject	Gender, age	Eye	Refraction	Visus c.c. (near)	Fixation	Strabismus (sim. cover test)	Stereo (TNO)	History
Anisomet	tropic amblyopes							
МК	Male, 51 years	RE	Plano + 2.50 RE/LE add +2.00	0.90	Central	Far 0°	Ø Titmus	Family history; first RX with 16 years
		LE*		0.16	Central	Near 0°	fly	
НМ-К	Female,	RE*	+4.00 -2.50/55° +2.75 -1.25/100° RE/LE	0.50	Central	Far O°	60′′	Family history; first RX with 21 years
	50 years	LE	add +1.75	1.00	Central	Near 0°		
AR	Female,	RE*	Plano (LASIK)	0.50	Central, unsteady	Far 0°	120''	First RX at 7 years;, occlusion therapy and pleoptics at 7–
	25 years	LE	Plano	1.00	Central	Near 0°		8 years for 1 years; LASIK at 24 years, RE (previous refraction error: +3.50 -4.75/9°)
FW	Female,	RE	-0.50 -1.25/175°	1.25	Central	Far 0°	60′′	First RX at 7 years; occlusion therapy from 7 years (RE)
	21 years	LE*	-3.50 -2.75/175°	0.70	Central	Near 0°		
FA	Male, 32 years	RE*	-4.75 -2.00/10°	0.80	Centrall	Far 0°	Ø	First RX with 14 years
	······, j - ····	LE	-2.25 -2.25/170°	1.00	Central	Near 0°		
Strahism	ic amblyopes	22	2.20 2.20/170	1100	central	i i cui o		
SG	Female	RE	+3.00 -0.75/124°	1.40	Central nasal	Far +13° +VD 3°	Ø	Squint detected at 3 years; first RX at 4 years; occlusion
	36 years	LE*	+3.50 -1.00/19°	0.04	Foveal rim, unsteady	Near +15° +VD 3°	-	therapy from 3 to \sim 8–9 years; left-handed
LP	Female,	RE	+0.50	1.00	Central temporal rim	Far –12½°	Ø	Congenital strabismus; occlusion therapy at 4–5 years; first
	36 years	LE*	+0.75	0.25	contrai temporar rim	+VD1° near ca. 0°	2	RX at 5–6 years; Turner syndrome
SS	Female,	RE*	Plano	0.32	Parafoveolar central	Far +3°	Ø	Congenital esotropia; surgery RE at ca. 2–3 years (x2);
33	42 years	LE	Plano	1.25		Near +3°	Ø	occlusion therapy at 4–6 years; glasses from 6 until 11 years
кк	Female,	RE*	+3.75	0.70	Central Central	Far +1°	Ø Titmus	Microstrabismus; occlusion therapy between 5 and 7 years;
ΝŇ		LE	+4.00	1.25	Celitral Celitral	Near +2°		first RX with 7 years
	20 years			0.80	Townsonal size control		fly Ø	
WB	Male, 20 years	RE* LE	+1.00 -0.25/0° + 0.25	1.25	Temporal rim central	Far —7° Near —10°	Ø	Childhood strabismus; first RX at 5 years; occlusion therapy from 4 to 6 years
	ic & anisometropi			0.000			~	
B-SB	Female,	RE*	-0.75	0.063	Temporal, nyst. central,	Far -3° +VD 2½°	Ø	Squint since birth; surgery at 20 months; first RX with
	32 years	LE	-1.75 -2.00/175°	0.90	nyst.	Near -3° +VD 2°		3 years; alternating occlusion therapy from 3 to 6 years
KB	Male, 45 years		+0.50 +2.50 -1.00/90°	1.250.125	Central parafoveolar	Far $-\frac{1}{2}^{\circ}$ $-$ VD $2\frac{1}{2}^{\circ}$	Ø Titmus	Family history; first RX ca. 10 years; occlusion & pleoptic
		LE				Near -5° –VD 3°	fly	therapy between 9 and 11 years
KF	Female,	RE	$-1.50 - 0.25/60^{\circ}$	1.00	Central	Far −19°	Ø	First RX with 3 years; occlusion therapy from 3 years to
	42 years	LE*	$0.00 - 0.50/0^{\circ}$	0.40	Central	Near $-17\frac{1}{2}^{\circ}$		school entry
K-HW	Male, 61 years	RE*	+5.50 -4.50/10° -0.75	0.63	Central	Far ca. 0°	Ø Titmus	Family history of anisometropia; first RX with 18 years
		LE	RE/LE add +2.50	1.00	Central	Near -1° +VD $1\frac{1}{2}^{\circ}$	fly	
KL	Female,	RE*	+1.00 -0.75/114°	0.70	Central, unsteady central	Far +1° +VD 11/2°	Ø Titmus	Very premature birth, respirator; congenital strabismus; first
	24 years	LE	-3.00 -0.50/61°	1.00		Near +1° +VD 1½°	fly	RX with 3 years; occlusion therapy from 3 to 7 years, surgery at 10 years
Strabism	ics with alternatin	ig fixat	ion					·
AL	Female,	RE	+2.25 -1.75/175°	1.40	Central nasal, unsteady	Far +3°	Ø	Family history; first RX at ca. 2 years; occlusion therapy from
	20 years	LE*	+4.50 -2.25/12°	1.40	•	Near +3°		2 to 3 years until ca. 12 years of age (RE)
LJ	Female,	RE	+0.50 -1.50/167°	1.00	Central, nyst.	Near +19° DVD 1½°	Ø	Family history; squint onset in infancy; first RX at 1 years;
5	22 years	LE*	-2.00 -2.25/175°	1.25	Central, nyst.	Far +14°		occlusion therapy from 1 years until school age; surgery at 18 months
RW	Male, 26 years	RE	+2.25 -0.75/155°	1.40	Central	Far +6°	Ø	Squint onset in infancy; first RX with 2 years, 2–3 surgeries;
	Maie, 20 years	LE*	+2.25 -0.75/155°	1.25	Central	Near +6° +VD 2°	5	occlusion therapy
FS	Female,	RE	Plano	1.25	Central	Far +2°	Ø	First RX at 2 years, surgery at 6 years; occlusion therapy from
	28 years	LE*	Plano	1.00	Central	Near +3°	<i>b</i>	2 years until school age
PG			Plano	1.40	Central	Far +5°	Ø	Initially large-angle strabismus; first RX at 6 years, worn for
	Wale, 22 years	LE*	Plano	1.40	Central	Near +6°	Ø	1 years; occlusion therapy at 5–7 years, two surgeries (both eves)
TC-F	Male, 28 years	RE	+1.25	1.25	Central	Far −15°	Ø	Squint from birth; first RX at 3 years; occlusion therapy at 2–
TG-F	wale, 28 years						Ø	
67	Ferrela	LE*	+0.75 -0.50/3°	1.40	Central	Near -15°	a	3 years (LE); surgery at 20 years (LE)
GZ	Female,	RE*	Plano	1.00	Central	Far -8°	Ø	Squint detected at 2 years, first RX with 2–3 years, occlusion
	25 years	LE	Plano	1.40	Central	Near -9°	a	therapy and pleoptics at 2–3 years
JM	Female,	RE*	+1.75	1.25	Central	Far -2°	Ø	First RX at 3 years of age, occlusion and pleoptic therapy at
	29 years	LE	-0.25/100° +1.75	1.40	Central	Near $-\frac{1}{2}^{\circ}$		3 years

In each etiology group, the subjects are arranged in ascending order of the visual acuity of the amblyopic eye. Abbreviations: RE, right eye; LE, left eye; VD, vertical deviation; +, esotropia, -, exotropia; *, non-dominant.

tive equivalence (PSE) represents the intersection of the psychometric curve with the *x*-axis.

The raw data and the resulting psychometric functions of one subject with a deep mixed amblyopia (B-SB) are exemplified in Fig. 1. In the left panels, the regions between the dark and light gray horizontal lines show the range of the step sizes over all trials of one condition. With the dominant eye, the subject bisects the line closer to the veridical middle of the line, with a variability range of 0.7° . In contrast, with the amblyopic eye, the subject bisects the line towards the right side; the variability range is 1.0° . The resulting psychometric functions (right panels in Fig. 1) indeed show a stronger rightward shift and a shallower slope of the psychometric function obtained with the amblyopic eye, consistent with the larger variability range.

2.3. Statistical analysis of the results

The results were illustrated by the cumulated psychometric functions (PFs) of the experimental groups, derived from the individual data obtained with the adaptive procedure. We used the psychometric functions solely as means to visualize the shift in line bisection and to enable a qualitative comparison of the results of this study with previous data obtained using the same procedure (Sireteanu et al., 2005, 2006). The quantitative analysis was based on the non-biased points of subjective equivalence (PSEs), averaged over all subjects in the different experimental groups.

Statistical evaluation of the group differences between the magnitude of the biases (PSEs) obtained with the different parameters was performed using a repeated-measures multivariate analysis of variance (MANOVA) model that included eye, length of the test line and presentation time as independent variables, and PSE (point of subjective equality) as dependent variable. Negative values of the PSEs indicate a leftward bias, positive values a rightward bias. We speak of a significant bias whenever the mean PSE of a group of experimental subjects differed significantly (p < .05) from the mean PSE of the normally sighted subjects.

3. Results

3.1. Experiment 1: monocular line bisection in normally sighted observers: the role of stimulus length and duration

As expected, normally sighted subjects showed a consistent leftward bias, when asked to bisect the horizontal lines. They overestimated the left part of the pretransected line, which means that they set the transector too far to the left. This leftward bias varied with the length of the line and with the duration of the stimulus: as for the binocular condition (see also Sireteanu et al., 2005), it was higher for longer lines and shorter durations, but it was highly statistically significant for all conditions (length: F(6) = 48.14; p < .001; duration: F(6) = 25.86; p < .001). Fig. 2 shows the averaged monocular psychometric curves of the group of normally sighted observers, under the different experimental conditions (upper panel: dominant eyes; lower panel: non-dominant eyes).

The mean monocular bias of the group of normal observers, averaged over conditions, was -0.16° for the dominant eyes and -0.24° for the non-dominant eyes. Both values differ statistically highly significantly form the veridical midpoint (dominant eyes:

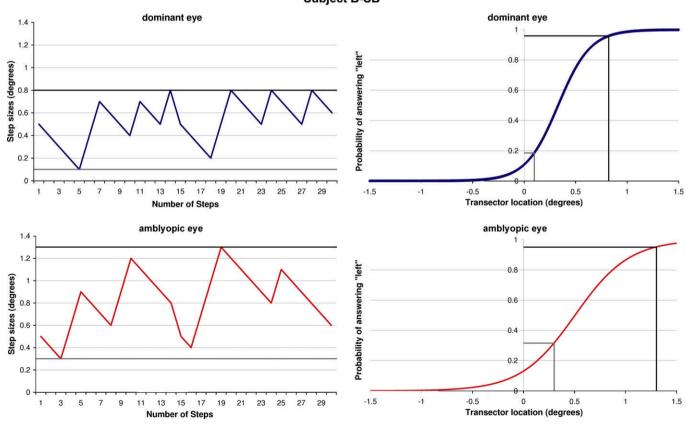


Fig. 1. Raw data and psychometric functions of one subject with mixed amblyopia (B-SB). Left panels: trial-by-trial responses for one condition (repetition after 15 trials). The regions between the dark and light gray horizontal lines show the range of the step sizes over all trials of this condition. Right panels: psychometric functions generated from the data in the left panels. Upper panels: dominant eye; lower panels: amblyopic eye.

Line Bisection Subject B-SB

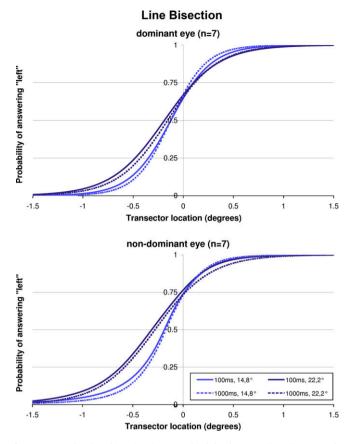


Fig. 2. Monocular line bisection in normal adult observers (n = 7). Monocular psychometric curves relating the cumulated probability of the subjects to answer "left" to the actual position of the transector. Upper panel: dominant eyes; lower panel: non-dominant eyes. Light blue curves: shorter lines (14.8°); dark blue curves: longer lines (22.2°). Continuous lines: stimuli are presented at shorter durations (100 ms); dotted lines: stimuli are presented at longer durations (1000 ms). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this paper.)

t(6) = -5.65; p < .001; non-dominant eyes: t(6) = -4.90; p < .001). The averaged bias was statistically significantly higher for the non-dominant than for the dominant eyes (F(1,6) = 4.72; p = .034). The overall leftward monocular bias, averaged over eyes and conditions, was -0.20° . This value differs statistically highly significantly from the veridical midpoint (F(6) = 6.71; p < .001) and is very close to the value determined binocularly for normally sighted adult observers tested under identical experimental conditions (-0.24° ; Sireteanu et al., 2005).

3.3. Experiment 2: monocular line bisection in experimental observers

The psychometric curves of all groups of experimental subjects, averaged over conditions, are shown in Fig. 3. For a comparison, the mean values of the normally sighted observers are replotted in each panel.

3.3.1. Purely anisometropic amblyopes

Purely anisometropic amblyopes showed consistent leftward biases in their dominant eyes. The cumulated psychometric curves showed a marked displacement (-0.40°) for the non-dominant eyes, and a smaller one for the amblyopic eyes (-0.11°). The difference to the normally sighted group was statistically significant for the dominant eyes (F(1,10) = 3.37; p = .007). For the amblyopic eyes, the mean settings showed a statistically significant rightward bias, when compared to the non-dominant eyes of the normally

sighted observers (F(1,10) = 7.64; p < .01; see left upper panel in Fig. 3).

3.3.2. Strabismic amblyopes without anisometropia

The dominant eyes of the group of *purely strabismic amblyopes* showed an almost veridical line bisection, while the amblyopic eyes showed a significant rightward bias. Mean PSE was -0.01° for the dominant and $+0.16^{\circ}$ for the amblyopic eyes. Both values differed statistically highly significantly from the mean settings of the normally sighted subjects (for the dominant eyes: F(1,10) = 10.66; p < .002; for the non-dominant eyes: F(1,10) = 8.98; p < .004). For both eyes, the psychometric curves were more shallow than in normally sighted observers (see right upper panel in Fig. 3).

3.3.3. Strabismic and anisometropic amblyopes

The mean settings through the dominant eyes of the subjects with mixed amblyopia did not depart from the veridical line bisection, thus showing a rightward deviation in comparison to the normally sighted observers. The subjects showed even more pronounced rightward deviations through the amblyopic eye than with the dominant eyes. Mean PSEs of the group were +0.0045° for the dominant and +0.19° for the amblyopic eyes (see left lower panel in Fig. 3). As for the purely strabismic amblyopes, the slopes of the psychometric curves were more shallow than in the normally sighted observers. The differences from the PSE values of the normally sighted subjects were statistically highly significant for both eyes (F(1,10) = 13.24; p < .001 for the dominant and F(1,10) = 25.57; p < .001 for the amblyopic eyes).

3.3.4. Strabismic subjects with alternating fixation

Both eyes of the strabismic subjects with alternating fixation showed a leftward bias from the veridical position, more pronounced in the non-dominant than in the dominant eyes (-0.18° in the dominant and -0.29° in the non-dominant eyes). These values do not differ significantly from those of the normally sighted observers (F(1,13) = 0.58; p = .45 for the dominant and F(1,13) = 1.11; p = .30 for the non-dominant eyes; see lower right panel in Fig. 3). Thus, as a group, strabismics with alternating fixation yielded results similar to those of the normally sighted subjects.

3.3.5. Comparison of the cumulated group data

The averaged PSEs of all groups of subjects are summarized in Fig. 4. Anisometropic amblyopes showed a consistent rightward deviation from the settings of the normally sighted observers, affecting only the amblyopic eyes. Significant rightward deviations occured in both eyes of strabismic amblyopes and of subjects with mixed amblyopia, in both cases much stronger in the amblyopic than in the dominant eyes. Subjects with alternating fixation did not differ significantly from normally sighted subjects.

4. General discussion

4.1. Evaluation of the results

Previous studies (Halligan & Marshall, 1992; McCourt, 2001; Sireteanu et al.,2005, 2006; von Helmholtz, 1896) have shown that, when asked to bisect a horizontal line, normally sighted adult observers show a consistent leftward bias. This effect was called "pseudoneglect". The results of our first experiment confirm and extend these results, by demonstrating that this effect occurs also with monocular vision. As with binocular vision, its magnitude depends on the parameters of the experiment. Overall, it can be said that the leftward bias is larger for the more difficult conditions (shorter durations, longer lines, non-dominant eyes). These results

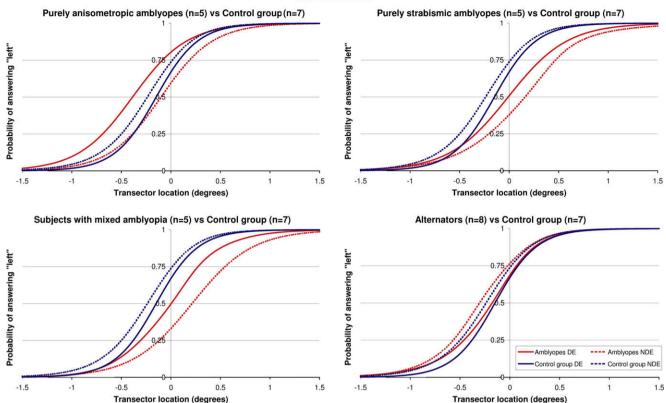


Fig. 3. Monocular line bisection in all subjects, averaged over conditions. Left upper panel: anisometropic amblyopes (n = 5); right upper panel: strabismic amblyopes (n = 5); left lower panel: strabismics with alternating fixation (n = 8). For comparison, each panel includes the psychometric curves of the normally sighted observers (n = 7).

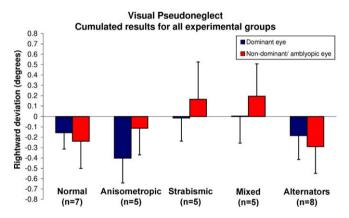


Fig. 4. Cumulated results for all experimental groups. On the ordinate: deviation from straight-ahead (PSEs). Negative values indicate a leftward deviation ("pseudo-neglect"); positive values indicate a rightward deviation. Relative rightward deviation indicates a "minineglect". Blue columns: dominant eyes; red columns: non-dominant eyes. Error bars indicate standard deviations of the mean. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this paper.)

cannot have been related to the handedness of the subjects, since all normally sighted observers included in this study were righthanded. They are also unlikely to have been to an ocular deficit of the tested subjects, since no consistent optical problems were observed in any of these subjects.

The results of the second experiment demonstrate that a consistent rightward bias occurs in both eyes of strabismic and strabismic-anisometropic subjects, while in anisometropic amblyopes the effect is present only in the amblyopic eyes. Consistent with the previous literature, we called this bias "minineglect" (Sireteanu et al., 2005, 2006). Strabismics with alternating fixation and good vision in each eye showed more variable results, but their mean bias showed a "pseudoneglect" similar to the normally sighted observers.

These results confirm our hypothesis that strabismic amblyopia is associated with a consistent, bilateral rightward bias in a line bisection task. This effect is reminiscent of the effect shown by neurological patients with visual attention deficits (neglect) and could therefore be defined as a "minineglect". This effect suggests the existence of a subtle, but reliable deficit in the orienting of spatial attention towards the extrapersonal space.

4.2. Possible neural mechanisms

Several hypotheses have been put forward to explain the spatial deficits in strabismic amblyopia, ranging from neural scrambling (Hess, 1982), neural undersampling (Levi & Klein, 1986), uncalibrated disarray of cells (Hess & Field, 1994), or intrinsic spatial disorder (Levi, Klein, Sharma, Nguyen, et al., 2000). Our findings can be explained only partially in terms of these hypotheses. While the larger spatial uncertainty manifested in the more shallow slope of the psychometric curves of the amblyopic subjects could be interpreted as an expression of neural disarray, an explanation of the consistent rightward bias in amblyopic subjects with a history of strabismus requires additional neural mechanisms.

The occurrence of a "minineglect" in amblyopic subjects with a history of strabismus suggests impairments in goal-directed attentional mechanisms, which are believed to be based on the activity of a network of cortical regions, including mainly regions on the dorsal visual pathway (Corbetta & Shulman, 2002; Kastner &

Line Bisection

Ungerleider, 2000). The dorsal, "vision-for-action" (as opposed to the ventral, "vision-for-perception"; Goodale, 1997) pathway was reported to include structures in the posterior parietal cortex and to extend to the dorsal prefrontal cortex (Courtney, Ungerleider, Keil, & Haxby, 1996; Wilson, Scalaidhe, & Goldman-Rakic, 1993). One interesting aspect of our results is the fact that, in amblyopes with a history of strabismus, not only the settings of the amblyopic, but also those of the fellow eyes show a consistent minineglect. This finding reinforces the suggestion that the amblyopic deficit might involve binocular regions of the posterior parietal cortex (cf. Ho et al., 2006).

Several neuroimaging studies demonstrated that the ventral visual pathway is impaired in strabismic amblyopes (cf. Lerner et al., 2006; Li, Dumoulin, Mansouri, & Hess, 2007a, 2007b; Muckli et al., 2006). Our results thus agree with previous suggestions (Ho & Giaschi, 2006; Ho et al., 2006; Simmers et al., 2006; but see Levi & Tripathy, 2006) suggest that structures on the dorsal visual pathway might also be impaired in amblyopic subjects, especially in connection with a history of strabismus.

The presence of a doral deficit in strabismic and strabismicanisometropic amblyopes agrees with our finding that the cortical representation of spatial order might be disorganized in these subjects (Sireteanu et al., 2008). The representation of spatial order in the human brain is believed to rely on the activity of regions in the posterior parietal cortex (Marschuetz, Reuter-Lorenz, Smith, Jonides, & Noll, 2006; Marschuetz & Smith, 2006).

4.3. Relationship to other neurodevelopmental disorders

The similarity of the effects described in this study with those found in children with developmental dyslexia (Sireteanu et al., 2005, 2006) deserve some comment. Indeed, it is quite perplexing to find the same pattern of deficits in subjects with a primarily reading deficit, but no visual impairments (developmental dyslexics) and subjects with a deeply impaired visual function, but no language deficit (strabismic amblyopia). This intriguing similarity suggests that solving the line bisection task involves common neural mechanisms, which might be affected in both ailments. Indeed, subjects in both groups might present with a deficit in the orienting of spatial attention. Similarities between strabismic amblyopia and developmental dyslexia were described with other higher-order visual functions, like contour integration and global motion, which also require spatial attention (Simmers & Bex, 2001; Simmers et al., 2003, 2006).

5. Conclusion

Amblyopic subjects with a history of strabismus show consistent rightward deviations in a line bisection task, which are similarly to those of developmental dyslexics. These results suggest that both groups of subjects show subtle attentional deficits, in addition to their specific—visual, respectively, reading—impairments. They indicate that partially overlapping neural pathways might be involved in the emergence of the different neurodevelopmental disorders.

Acknowledgments

We thank Wolf Singer for support, Ralf Goertz for developing the software for running the experiments, Iris Bachert, Doris Baldauf, Peggy Feige, and Licia Cirina for the orthoptic examination of the subjects, and the participants in this study for their patience. The study was supported by grants from the Deutsche Forschungsgemeinschaft to Ruxandra Sireteanu (SI 344/17-1,2,3).

References

- Barnes, G. R., Hess, R. F., Dumoulin, S. O., Achtmann, R. L., & Pike, G. B. (2001). The cortical deficit in humans with strabismic amblyopia. *Journal of Physiology*, 533, 281–297.
- Barrett, B., Pacey, I. E., Bradley, A., Thibos, L., & Morill, P. (2003). Nonveridical visual perception in human amblyopia. *Investigative Ophthalmology & Visual Science*, 44, 1555–1567.
- Bäumer, C., & Sireteanu, R. (2006). Temporal instability in the perception of strabismic amblyopia. *Strabismus*, 14, 1–6.
- Bedell, H., & Flom, M. (1983). Normal and abnormal space perception. American Journal of Optometry & Physiological Optics, 60, 426–435.
- Bowers, D., & Heilman, K. M. (1980). Pseudoneglect: Effect of hemispace on a tactile line bisection task. Neuropsychologia, 18, 491–498.
- Bradshaw, J. L., Nettleton, N. C., Wilson, L. E., & Bradshaw, C. S. (1977). Line bisection by left-handed preschoolers: A phenomenon of symmetrical neglect. *Brain and Cognition*, 6, 377–385.
- Chockron, S., & De Agostini, M. (1995). Reading habits and line bisection: A developmental approach. Cognitive Brain Research, 3, 52–58.
- Chockron, S., & Imbert, M. (1993). Influence of reading habits in line bisection. Cognitive Brain Research, 1, 219–222.
- Corbetta, M., & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. Nature Reviews of Neuroscience, 3, 201–215.
- Courtney, S. M., Ungerleider, L. G., Keil, K., & Haxby, J. V. (1996). Object and spatial visual working memory activate separate neural systems in human cortex. *Cerebral Cortex*, 6, 39–49.
- Fronius, M., & Sireteanu, R. (1989). Monocular geometry is selectively distorted in the central field of strabismic amblyopes. *Investigative Ophthalmology & Visual Science*, 30, 2034–2044.
- Fronius, M., & Sireteanu, R. (1992). Lokalisationsstörungen bei Schielamblyopen: Horizontale Streckenteilung und vertikale relative Lokalisation. Klinische Monatsblätter der Augenheilkunde, 201, 22–29.
- Fronius, M., & Sireteanu, R. (1994). Pointing errors in strabismic amblyopes: Complex patterns of distorted visuomotor coordination. *Vision Research*, 34, 689–707.
- Goertz, R., & Sireteanu, R. (submitted for publication). Neurologically normal adult subjects show an auditory pseudoneglect.
- Goodale, M. A. (1997). Visual routes to perception and action in the cerebral cortex. In F. Boller, J. Grafman (Eds.), *Handbook of neuropsychology*, (Vol. 11, pp. 91– 109).
- Habib, M. (2000). The neurological basis of developmental dyslexia. An overview and working hypothesis. Brain, 123, 2372–2399.
- Halligan, P. W., Manning, L., & Marshall, J. C. (1991). Hemispheric activation vs spatio-motor cueing in visual neglect: A case study. *Neuropsychologia*, 29, 165–176.
- Halligan, P. W., & Marshall, J. C. (1992). Left visuo-spatial neglect: A meaningless entity? Cortex, 28, 525–535.
- Heilman, K. M. (1979). Neglect and related disorders. In K. L. Heilman & E. Valenstein (Eds.), *Clinical neuropsychology* (pp. 268–307). Oxford University Press.
- Heilman, K. M., Watson, R. T., & Valenstein, E. (1985). Neglect and related disorders. In K. M. Heilman & E. Valenstein (Eds.), *Clinical neuropsychology* (pp. 243–293). New York: Oxford University Press.
- Hess, R. F. (1982). Developmental sensory impairment: Amblyopia or tarachopia? Human Neurobiology, 1, 17–29.
- Hess, R., Campbell, F., & Greenhalgh, T. (1978). On the nature of the neural abnormality in human amblyopia: Neural aberrations and neural sensitivity loss. *Pfluegers Archiv*, 377, 201–207.
- Hess, R. F., & Field, D. J. (1994). Is the spatial deficit in strabismic amblyopia due to loss of cells or uncalibrated disarray of cells. *Vision Research*, 34, 3397–3406.
- Ho, C. S., & Giaschi, D. E. (2006). Deficient maximum motion displacement in amblyopia. Vision Research, 46, 4595–4603.
- Ho, C. S., Paul, P. S., Asirvatham, A., Cavanagh, P., Cline, R., & Giaschi, D. E. (2006). Abnormal spatial selection and tracking in children with amblyopia. *Vision Research*, 46, 3274–3283.
- Kaernbach, C. (1991). Simple adaptive testing with the weighted up-down method. Perception & Psychophysics, 49, 227–229.
- Kaernbach, C. (2001). Slope bias of psychometric function derived from adaptive data. Perception & Psychophysics, 63(8), 1389–1398.
- Karnath, H.-O., Ferber, S., & Himmelbach, M. (2001). Spatial awareness is a function of the temporal not the posterior parietal lobe. *Nature*, 411, 950–953.
- Kastner, S., & Ungerleider, L. G. (2000). Mechanisms of visual attention in the visual cortex. Annual Review of Neuroscience, 23, 27–43.
- Lagrèze, W.-D., & Sireteanu, R. (1991). Two-dimensional spatial distortions in human strabismic amblyopia. Vision Research, 31, 1271–1288.
- Lerner, Y., Hendler, T., Malach, R., Harel, M., Leiba, H., Stolowitch, C., et al. (2006). Selective fovea-related deprived activation in retinotopic and high-order visual cortex of human amblyopes. *NeuroImage*, 33, 169–179.
- Levi, D., & Carkeet, A. (1993). Amblyopia: A consequence of abnormal visual development. In K. Simons (Ed.), *Early visual development normal and abnormal* (pp. 391–408). New York: Oxford University Press.
- Levi, D. M., & Klein, S. A. (1986). Sampling in spatial vision. Nature, 320, 360-362.
- Levi, D. M., Klein, S. A., Sharma, V., & Nguyen, L. (2000). Detecting disorder in spatial vision. Vision Research, 40, 2307–2327.

- Levi, D. M., & Tripathy, S. P. (2006). Is the ability to identify deviations in multiple trajectories compromised in amblyopia? *Journal of Vision*, 6, 1367–1379.
- Li, X., Dumoulin, S. O., Mansouri, B., & Hess, R. F. (2007a). Cortical deficits in human amblyopias: Their regional distribution and their relationship to the contrast detection deficit. *Investigative Ophthalmology & Visual Science*, 48, 1575–1591.
- Li, X., Dumoulin, S. O., Mansouri, B., & Hess, R. F. (2007b). The fidelity of the cortical retinotopic map in human amblyopia. *European Journal of Neuroscience*, 25, 1265–1277.
- Marschuetz, C., Reuter-Lorenz, P. A., Smith, E. E., Jonides, J., & Noll, D. C. (2006). Working memory for order and the parietal cortex: An event-related functional magnetic resonance imaging study. *Neuroscience*, 139, 311–316.
- Marschuetz, C., & Smith, E. E. (2006). Working memory for order: Multiple cognitive and neural mechanisms. *Neuroscience*, 139, 195–200.
- McCourt, M. (2001). Performance consistency of normal observers in forced-choice tachistoscopic visual line bisection. *Neuropsychologia*, 39, 1065–1076.
- McKee, S., Levi, D., & Movshon, T. (2003). The pattern of visual deficits in amblyopia. *Journal of Vision*, 3, 380-405.
- Muckli, L., Kiess, S., Tonhausen, N., Singer, W., Goebel, R., & Sireteanu, R. (2006). Cerebral correlates of impaired grating perception in individual, psychophysically assessed human amblyopes. *Vision Research*, 46, 506–526.
- Pisella, L., & Mattingley, J. B. (2004). The contribution of spatial remapping impairments to unilateral visual neglect. *Neuroscience and Biobehavioural Reviews*, 28, 181–200.
- Scarisbrick, D. J., Tweedy, J. R., & Kulanski, G. (1987). Hand preference and performance effects in line bisection. *Neuropsychologia*, 25, 695–699.
- Schelchshorn, J., Yoo, M. H., Chung, C. S., & Sireteanu, R. (1998). Visual asymmetries in the perception of simultaneously presented objects. *Perception*, 27(Suppl.), 165.
- Schenkenburg, T., Bradford, D., & Ajax, E. (1980). Line bisection and unilateral neglect in patients with neurologic impairment. *Neurology*, 30, 509–517.
- Simmers, A., & Bex, P. J. (2001). Deficits in contour integration in dyslexia. Investigative Ophthalmology & Visual Science, 42, 2737-2742.

- Simmers, A. J., Ledgeway, T., Hess, R. F., & McGraw, P. V. (2003). Deficits to global motion processing in human amblyopia. *Vision Research*, 43, 729–738.
- Simmers, A. J., Ledgeway, T., Mansouri, B., Hutchinson, C. V., & Hess, R. F. (2006). The extent of the dorsal extra-striate deficit in amblyopia. *Vision Research*, 46, 2571–2580.
- Sireteanu, R. (2000). The binocular act in strabismus. In G. Lennerstrand & Y. Ygge (Eds.), Advances in strabismus research: Basic and clinical aspects (pp. 63–83). London, UK: Portland Press Ltd.
- Sireteanu, R., Bäumer, C., Sârbu, C., & Iftime, A. (2007). Spatial and temporal misperceptions in amblyopic vision. *Strabismus*, *15*, 45–54.
- Sireteanu, R., & Fronius, M. (1989). Monocular geometry is selectively distorted in the central visual field of strabismic amblyopes. *Investigative Ophthalmology & Visual Science*, 30, 2034–2044.
- Sireteanu, R., Goebel, C., Goertz, R., & Wandert, T. (2006). Do children with developmental dyslexia show a selective visual attention deficit? *Strabismus*, 14, 85–93.
- Sireteanu, R., Goertz, R., Bachert, I., & Wandert, T. (2005). Children with developmental dyslexia show a left visual "minineglect". Vision Research, 45, 3075–3082.
- Sireteanu, R., Lagrèze, W.-D., & Constantinescu, D. H. (1993). Distortions in twodimensional visual space perception in strabismic observers. *Vision Research*, 33, 677–690.
- Sireteanu, R., Thiel, A., Fikus, S., & Iftime, A. (2008). Patterns of spatial distortions in human amblyopia are invariant over presentation time and stimulus modality. *Vision Research*, 48, 1150–1163.
- Vallar, G., & Perani, D. (1986). The anatomy of unilateral neglect after righthemisphere stroke lesions. A clinical/CT-scan correlation study in man. *Neuropsychologia*, 24, 609–622.
- von Helmholtz, H. (1896). Handbuch der Physiologischen Optik (2. Aufl.). Hamburg: Voss.
- Wilson, F. A., Scalaidhe, S. P., & Goldman-Rakic, P. S. (1993). Dissociation of object and spatial processing domains in the primate prefrontal cortex. *Science*, 260, 1955–1958.