Ocular dominance in extrastriate cortex of strabismic amblyopic cats

Jan-Hinrich Schröder a,*, Pascal Fries a,b,1, Pieter R. Roelfsema a,2, Wolf Singer a and Andreas K. Engel a,3

a Max Planck Institute for Brain Research, Deutschordenstraße 46, 60528 Frankfurt, Germany
b Department of Psychiatry I, Johann Wolfgang Goethe University, Heinrich-Hoffmann-Straße 10, 60528 Frankfurt, Germany

Abstract

Ocular dominance in extrastriate visual cortex of cats with behaviorally defined strabismic amblyopia was studied using extracellular recording techniques. In area 18, the amblyopic eye drove about as many cells as the normal one. In area posteromedial lateral suprasylvian area (PMLS), about 60% of the cells responded exclusively to stimulation of the normal eye and 30% to stimulation of the amblyopic eye. In area 21a more than 75% of the cells were monocularly driven by the non-amblyopic eye while only 5% were monocularly driven by the amblyopic eye. These findings suggest that ventral pathways (area 21a) are more affected in amblyopia than dorsal pathways (area PMLS).

Keywords

Amblyopia; Area 21a; Extrastriate; Ocular dominance; Strabismus
Amblyopia is defined by a decrease of visual acuity for which no organic causes can be detected by physical examination of the eye. In the case of strabismus, amblyopia results if subjects continuously suppress the signals arriving from the same eye in order to avoid double vision (e.g. von Noorden, 1990). In addition to the reduction in visual acuity, strabismic amblyopia is associated with a variety of other deficits. The image conveyed by the amblyopic eye is temporally unstable (Altmann & Singer, 1986; Hess, Campbell, & Greenhalgh, 1978a) and spatially distorted (Lagrèze & Sireteanu, 1991; Sireteanu, Lagrèze, & Constantinescu, 1993). Subjects tend to mislocate targets (Hess & Holliday, 1992) and make false conjunctions between stimulus elements (Hess et al., 1978a). Another deficit typically encountered in this condition is the so-called crowding phenomenon, i.e., a deterioration of the ability to discriminate figures if they are surrounded by other contours (e.g. von Noorden, 1990).

Evidence from psychophysics has led to the conclusion that the deficit is situated in the visual cortex (Hess & Pointer, 1985; Levi & Klein, 1985). In a more detailed search for the physiological basis of amblyopia, several animal models have been investigated. Hubel and Wiesel (1965a) reported that following induction of strabismus cells in cat area 17, the primary visual cortex, had become monocular and that the two eyes were represented about equally in each hemisphere. Later studies confirmed this result but some of them revealed an additional slight bias in ocular dominance (OD) favoring the non-operated eye (Berman & Murphy, 1982; Freeman & Tsumoto, 1983; Sireteanu & Best, 1992; Yinon, Auerbach, Blank, & Friesenhausen, 1975). Various studies have reported decreased spatial resolution of striate cortical neurons in strabismic cats (Chino, Shansky, Jankowski, & Banser, 1983; Crewther & Crewther, 1990). Taken together, the correlates of amblyopia in area 17 were subtle and not consistent across studies. Note that in this respect strabismic amblyopia strongly differs from the form caused by monocular deprivation, which leads to a almost complete decoupling of the deprived eye (Hubel & Wiesel, 1970) and a profound loss of visual function.

In the monkey, the search for a cortical substrate of strabismic amblyopia has been confined to area V1. Kiorpes, Kiper, O'Keefe, Cavanaugh, and Movshon (1998) found that the two eyes were about equally effective in driving cortical cells but neurons driven by the amblyopic eye had reduced spatial resolution. However, optimal spatial frequency and peak contrast sensitivity of these neurons were better than expected from behavioral examination. From this the authors concluded that a full account of the physiological basis of amblyopia would require the investigation of processing stages beyond striate cortex (for a review see Kiorpes & McKee, 1999). In the present study, we have therefore measured neuronal response properties in various areas of the visual cortex of strabismic cats which had developed amblyopia.

Two previous studies have examined the effect of strabismus on neuronal response synchronization in the striate cortex of strabismic cats. The first one has demonstrated that in exotropic cats synchronization between monocular cells connected to different eyes is drastically reduced in comparison to synchronization among cells driven from the same eye (König, Engel, Löwel, & Singer, 1993). Synchronization among binocular cells could not be measured due to the low incidence of these cells in strabismic animals. The second study, conducted in esotropic amblyopic cats, revealed that response synchronization is reduced among neurons
driven by the amblyopic eye as compared to those driven by the normal eye, in particular when responses are evoked by gratings with high spatial frequency (Roelfsema, König, Engel, Sireteanu, & Singer, 1994). Quite unexpectedly, no significant differences were found in the spatial resolution and response vigor of cells driven by the normal and the amblyopic eye, suggesting reduced synchronization as a major cause of the amblyopic deficit. It has been proposed that synchronization raises the saliency of responses due to enhanced summation of excitatory synaptic potentials in target cells (Niebur, Koch, & Rosin, 1993), and recent experimental (Alonso, Usrey, & Reid, 1996; Brecht, Singer, & Engel, 1998) and theoretical (Lumer, Edelman, & Tononi, 1997; Stevens & Zador, 1998) evidence is compatible with this suggestion. This predicts that changes in response synchronization at one level of processing lead to changes in discharge rate at the next processing stage. The amblyopic deficit should then be associated with reduced responses to the amblyopic eye at processing stages beyond primary visual cortex. Here we examine this prediction by analyzing responses in areas 18 and 21a and posteromedial lateral suprasylvian (PMLS) of amblyopic cats. Preliminary data have been published in abstract form (Schröder, Fries, Roelfsema, Singer, & Engel, 1998).

2. Methods

All experimental procedures comply with European and NIH standards on the welfare of animals. This report is based on six cats in which convergent strabismus had been induced under general ketamine/xylazine anesthesia (10 and 2 mg/kg, respectively) by transecting the lateral rectus muscle of the right eye at an age of three weeks. The angle of the resulting convergent squint was determined repeatedly during development using the corneal reflex method (Sherman, 1972; Von Grünau, 1979). Several flashlight snapshots of the animal's head were taken and the ratio of the distance of the corneal reflexes over the distance of the pupils was determined on the photoprints. This ratio provides a measure of the strabismic angle.

At the age of 4–5 months, the animals were mildly food deprived and trained to discriminate between a square wave grating and equiluminant gray (Teller Acuity Cards, contrast 82–84%, luminance 25 cd/m²) on a jumping stand (Katz & Sireteanu, 1992; Mitchell, Griffin, Wilkinson, Anderson, & Smith, 1976). Jumps to the grating were rewarded (correct response). A session continued until the cat stopped jumping spontaneously. After sufficient training, cats were tested through the normal and the deviating eye on alternate days, the respective other eye being occluded by an opaque contact lens during testing. Thus, it was possible to assess visual acuity for the two eyes independently by variation of the spatial frequency of the gratings (0.21–14.2 cycles per degree with intervals of 0.5 octaves). Each eye was tested on at least three different days with a minimum of 180 jumps altogether. The spatial frequency of the cards was continuously adjusted to the performance of the animal.

Discrimination threshold was defined as the spatial frequency at which the animal performed at the 75% level (chance level: 50%). The psychometric functions resulting from the behavioral testing were fitted by the function

\[ P(x) = 0.5 + 0.5 \left[ 1 + \left( \frac{x}{a} \right)^b \right]^{-1} , \]

where \( P \) denotes performance, \( x \) spatial frequency, \( a \) discrimination threshold and \( b \) slope at threshold. For the discrimination thresholds of the two eyes 95% confidence intervals were calculated using a Monte Carlo simulation. Animals were considered to be amblyopic if the
discrimination thresholds of the two eyes differed by at least half an octave and if the confidence intervals for the respective discrimination thresholds were non-overlapping. For subsequent physiological measurements we selected four cats which were amblyopic according to these criteria. The animals included in this study were chosen from a larger cohort of amblyopic cats and have been selected for similar and relatively small differences in acuity between the two eyes which corresponds to mild amblyopia. Two additional strabismic cats that had been classified as non-amblyopic after behavioral testing served as controls. We used standard surgical and recording techniques. Anesthesia was induced by intramuscular injection of ketamine and xylazine (10 and 2 mg/kg, respectively) and maintained by ventilating the animal with a mixture of 70% N₂O, 30% O₂ and 0.8–1.2% halothane. After craniotomy and induction of paralysis (pancuronium bromide, 0.15 mg/(kg h)), the activity of single cells and small multiunit clusters was recorded extracellularly in areas 18, 21a and the PMLS area using tungsten microelectrodes. The areas were defined according to the stereotactic coordinates of Tusa and coworkers (Palmer, Rosenquist, & Tusa, 1978; Tusa & Palmer, 1980; Tusa, Rosenquist, & Palmer, 1979). In most of the experiments, electrode tracks were reconstructed histologically after transcardial perfusion and Nissl staining. The electrode signals were amplified, band-pass filtered and fed through a Schmitt trigger to obtain TTL pulses which signaled spike timing. Receptive fields (RFs) and neuronal response properties were assessed with hand-held stimuli. In addition, the OD was examined quantitatively by monocular stimulation of the two eyes with moving light bars of optimal length, width, orientation, direction and velocity. In cases where mapping with hand-held stimuli revealed a clear response upon stimulation of one of the eyes but failed to reveal any response through the respective other eye, quantitative measurements were omitted.

In order to classify recording sites with respect to OD we defined five OD classes. OD 1 and 5 were assigned to monocular responses obtained by left or right eye stimulation, respectively. Binocular responses were classified as OD 3. If a given recording site responded to stimulation through one eye at least twice as strongly as to stimulation through the other eye it was assigned OD 2 or 4, depending on which eye was dominating. The significance of the most prominent feature of the OD distributions, their bias favoring one of the two eyes, was tested against the null hypothesis of an equal distribution of left and right eye monocular cells by applying a test based on the cumulative binomial distribution. For this purpose, OD distributions were simplified by dividing recording sites in only two groups: sites dominated by the left (OD 1 and 2) and the right (OD 4 and 5) eye. Because of the very low incidence (about 5%) of balanced binocular recording sites (OD 3) in our cats it seemed justified to exclude these from statistical analysis. All p values given in this paper refer to this significance test.

3. Results

3.1. Squint induction
The corneal reflex method indicated that induction of convergent strabismus had been effective in all our animals. The ratio of the distance of the pupils over the distance of the reflexes ranged from 0.97 to 1.03 (Table 1) which has to be compared to 0.954±0.007 (SD), the value for normal animals more than two months old (Von Grünau, 1979).
Table 1 Behavioral data of the six cats used in the study

<table>
<thead>
<tr>
<th>Cat</th>
<th>Ratio (reflexes/pupils)</th>
<th>Threshold of the non-deviated eye</th>
<th>Threshold of the deviated eye</th>
<th>Acuity difference (octaves)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.03±0.01</td>
<td>2.07 (1.66–2.79)</td>
<td>1.19 (0.87–1.86)</td>
<td>0.80</td>
</tr>
<tr>
<td>2</td>
<td>0.99±0.01</td>
<td>2.19 (1.91–2.71)</td>
<td>1.36 (1.2–1.6)</td>
<td>0.69</td>
</tr>
<tr>
<td>3</td>
<td>1.01±0.002</td>
<td>1.68 (1.36–2.23)</td>
<td>1.04 (0.88–1.36)</td>
<td>0.69</td>
</tr>
<tr>
<td>4</td>
<td>1.02±0.005</td>
<td>1.47 (1.35–1.65)</td>
<td>0.92 (0.79–1.07)</td>
<td>0.68</td>
</tr>
<tr>
<td>5</td>
<td>1.00±0.03</td>
<td>2.35 (1.91–3.13)</td>
<td>2.86 (2.3–3.93)</td>
<td>-0.28</td>
</tr>
<tr>
<td>6</td>
<td>0.97±0.005</td>
<td>2.1 (1.7–2.6)</td>
<td>1.9 (1.6–2.4)</td>
<td>0.14</td>
</tr>
</tbody>
</table>

In the second column, the ratios of reflex distance over pupil distance on the photoprints are reported. In the third and fourth column the acuities measured as discrimination thresholds in the jumping stand procedure are given in cycles per degree for the left (non-deviated) and the right (deviated) eye. The numbers in brackets indicate 95% confidence intervals as determined by a Monte Carlo simulation. The difference in acuity is expressed in octaves in the fifth column.

3.2. Assessment of amblyopia

The behavioral performance of cats 1–4 is shown in Fig. 1. All animals were able to discriminate higher spatial frequencies with the non-operated eye than with the deviating eye. The discrimination thresholds differed by about 0.7 octaves. With the exception of cat 1, the 95% confidence intervals of the discrimination thresholds were non-overlapping. Thus, cats 2, 3 and 4 satisfied our criteria of significance (Table 1) and were classified as amblyopic. It might be argued that cat 1 cannot be considered amblyopic because of the slight overlap of the confidence intervals. However, as the OD of recording sites in cat 1 was consistent with those in cats 2–4 we decided not to exclude these data from our sample. In the control animals (cats 5 and 6), by contrast, the interocular difference in visual acuity was much smaller than in cats 1–4 and far from significant (see Fig. 4a and b).
Figure 1 Behaviorally determined visual acuity of amblyopic cats. Performance with the non-operated left eye and the operated right eye is shown by squares and triangles, respectively. Error bars indicate the standard error of the mean. Performance was fitted by a sigmoid function. The dashed line refers to the 75% level of performance, which was taken as a criterion for the discrimination threshold. Light and dark rectangles on the abscissa denote the 95% confidence intervals of discrimination thresholds for the non-operated and the operated eye which were determined by a Monte Carlo simulation.

3.3. Ocular dominance
Data were obtained from 511 multi-unit clusters or single units along 109 independent penetrations distributed over three areas (18, PMLS, 21a) in all eight hemispheres of the four amblyopic cats. RFs were typically located within the central 15° of visual angle. In most cases cells responded strongly to visual stimuli and, therefore, orientation preference, direction preference and, most importantly, OD could be determined reliably. Parameters like RF location and size, orientational tuning for light bars, preferred direction of moving stimuli and OD typically changed along the electrode tracks, sometimes continuously, sometimes abruptly. This reflects the fact that electrodes penetrated obliquely to the cortical surface, thus traveling through different columns. An example of the RF sequence in a typical penetration is illustrated in Fig. 2.
In general, about 80% of the recording sites in all areas under study responded monocularly (Fig. 3a). In area 18 of the amblyopic cats 1–4, the vast majority (approximately 75%) of the cells in both hemispheres responded exclusively to visual stimulation of the contralateral eye (Fig. 3a). Superimposed on this effect was a weak bias towards the normal eye (the left eye in all cats). In the hemisphere contralateral to the normal eye (right hemisphere) this bias was adding to and in the other hemisphere it was reducing the prevalence of the respective contralateral eye.

**Figure 2** Example of a sequence of RFs along an electrode track in area 21a, left hemisphere. Numbers in the RFs denote the penetration depth of the electrode and the OD at the penetration site. Arrows indicate the preferred direction of movement of a visual stimulus. Note the variability of RF properties and OD along the electrode track. ACL and ACR indicate the projection of the area centralis of the left and right eye, respectively. The distance of the areae centrales was much larger than shown here: After induction of paralysis this cat (3) showed a squint angle of about 31°. The inset on the lower right illustrates the changes of OD along the recording tracks.

**Figure 3** OD distributions summed up across cats 1–4. (a) Numbers on the ordinate indicate the percentage of cells in each OD class. L and R, left and right hemisphere. Note the low incidence of binoc-
ular responses. In areas 18 and PMLS the respective contralateral eye is overrepresented, while in area 21a there is a bias favoring the left, non-amblyopic eye. (b) Control for the independence of sites recorded within the same penetration (details see Section 3). Note the similarity between the OD graphs in a and b.

The relative strength of these two effects was somewhat shifted in area PMLS, the trend towards the normal eye being slightly more pronounced than in area 18. The normal eye dominated all of the monocular cells in the contralateral (right) hemisphere and about 40% of them in the ipsilateral (left) hemisphere (Fig. 3a).

In area 21a, we obtained a strikingly different result: In both hemispheres, more than 75% of the cells responded exclusively to visual stimulation of the normal (left) eye (OD class 1) without displaying any response to stimulation of the amblyopic eye. In this area, only 5% of the recording sites were monocularly driven by the amblyopic (right) eye (OD class 5). The remaining 20% of the neurons in area 21a responded binocularly (Fig. 3a).

The OD distributions of area 18 (left and right hemisphere), area PMLS (right) and area 21a (left and right) differed from an even distribution at the level of $p<0.001$ and the distribution in area PMLS of the left hemisphere at a level of $p=0.024$.

In area 18 (Cynader, Gardner, & Mustari, 1984) and in lateral suprasylvian cortex (Sireteanu & Best, 1992) of strabismic cats some of the few remaining binocular cells have been found to exhibit anomalous retinal correspondence. The retinal positions of the RFs in the eyes were shifted so that they remained superimposed despite the strabismic angle. We have examined our data for the occurrence of this rare phenomenon but found no case of anomalous correspondence in any of the analyzed areas. A likely reason is that the animals examined here had developed amblyopia which implies that they had a strong preference for one eye and did not strive to preserve binocular functions. Other reasons could be differences in the amplitude of squint angle and in eye motility between the present and those previous studies.

3.4. Controls

For the quantification of OD distributions we counted the recording sites with a certain OD across all penetrations and expressed these numbers in percent of the total number of sites analyzed in a particular area and hemisphere (Fig. 3a). To control for the independence of the results from different sites along the same electrode tracks, we also determined separately OD distributions for single electrode tracks and normalized them to the number of analyzed sites. Subsequently, distributions were calculated across penetrations and across all amblyopic cats (cats 1–4) by summing up the normalized single-track distributions, thereby assigning the same weight to each penetration. OD distributions obtained in this way did not differ substantially from those obtained with the standard procedure (Fig. 3b). Thus, results from different recording sites can be regarded as being sufficiently independent from each other.

In all amblyopic cats (1–4) it was the operated eye that had become amblyopic. In order to exclude an effect of surgery per se on OD distributions we examined two cats (5 and 6) which had undergone unilateral surgery like the others but had not become amblyopic (Fig. 4a and b). These cats, too, exhibited a significant overrepresentation of the non-operated eye in area 21a of both hemispheres ($p<0.01$; Fig. 4c). However, in both cats, this OD shift was much
less pronounced than in the amblyopic animals (Fig. 4d). The proportion of cells dominated by the operated eye (OD 4 and 5) was about three times the one found in amblyopic cats (28% vs. 9%). From our results in cats 1–4 we were able to predict the proportions of cells that should have been dominated by the operated and the normal eye in cats 5 and 6 assuming the null hypothesis that the latter had exhibited the same degree of amblyopia. The deviation of the measured OD distributions from this prediction was highly significant (p<0.001), suggesting that the skewed OD in area 21a reflects the degree of amblyopia and not only unilateral surgery.

In all cases where histological reconstructions of electrode tracks were obtained these confirmed that recording sites had indeed been located in the targeted areas.
4. Discussion

4.1. Visual acuity
The visual acuity values obtained for our cohort of esotropic cats are similar to those determined in several previous studies (Holopigian & Blake, 1983; Jacobson & Ikeda, 1979; Mower & Duffy, 1983; Von Grünau & Singer, 1980). The acuity values for the non-deviating eye (averaging 1.94 cycles/degree) were lower than values reported for a group of normal cats that had been tested in the same apparatus (3.1 cycles/degree in Katz & Sireteanu, 1992). This is in accordance with other published demonstrations of reduced visual acuity in strabismic animals (Holopigian & Blake, 1983). However, the acuity values reported in the present study are also below those found by Crewther, Crewther, and Cleland (1985) and Mitchell, Ruck, Kaye, and Kirby (1984) in cats with strabismic amblyopia. With all likelihood, this difference can be ascribed to differences in the testing and reinforcement paradigms. We varied spatial frequencies rapidly and always included suprathreshold stimuli, while Crewther et al. (1985) and Mitchell et al. (1984) presented the same spatial frequencies on blocks of trials, allowing the animal to adjust its effort to the task difficulty.

4.2. Ocular dominance in amblyopic and normal cats
In this study OD was assessed from multi-unit rather than single-unit data and this has most likely led to an overestimation of binocular units. A recording site got only classified as monocular if all of the simultaneously recorded neurons were monocular. By contrast, only one or a few binocular cells would have led to a classification of the site as binocular even if the majority of the cells had been monocular.

In the present study, most neurons in the examined areas were monocular, which is consistent with earlier findings in areas 18 (Chino, Ridder, & Czora, 1988; Cynader et al., 1984) and PMLS (Sireteanu & Best, 1992) of strabismic cats. In contrast to area 17, where OD distributions tend to be U shaped in both hemispheres of strabismic cats (e.g. Hubel & Wiesel, 1965a), OD in area 18 exhibited a strong bias towards the respective contralateral eye, that was superimposed on a weak trend towards the normal eye. Results in area PMLS resembled those in area 18 except that the trend favoring the non-amblyopic eye was more pronounced. This is in accordance with the results of Sireteanu and Best (1992), who had examined prestriate areas in strabismic cats, however, without testing for amblyopia. Von Grünau (1982), by contrast, reported that binocularity was largely conserved in the LS areas of strabismic cats. The reason for this discrepancy is most likely that in his study squint was induced at the age of six to nine weeks rather than at three weeks as in our study.

In sharp contrast to the OD distributions in areas 17 (e.g. Roelfsema et al., 1994) and 18 which are either U shaped or biased towards the contralateral eye, the distributions in area 21a were strongly biased towards the normal eye. As suggested by the much more symmetrical distribution in the squinting control cats that had no interocular difference in visual acuity, this marked loss of responses to stimulation of the deviated eye is most likely due to the development of amblyopia. Our data do not allow us to determine whether the weak bias in the
control cats is related to mild amblyopia that was not accompanied by detectable acuity changes or whether it is solely related to strabismus.

OD differs across areas also in normal cats. First, the percentage of monocular cells decreases from 15–30% to 5–10% as one proceeds from primary areas 17 (Dreher, Michalski, Ho, Lee, & Burke, 1993; Hubel & Wiesel, 1965a; Sireteanu & Best, 1992) and 18 (Cynader et al., 1984; Dreher et al., 1993; Hubel & Wiesel, 1965b) to prestriate areas PMLS (Hubel & Wiesel, 1969; Sireteanu & Best, 1992; Spear & Baumann, 1975) and 21a (Dreher et al., 1993). Second, while the two eyes are represented equally in area 17, the contralateral eye dominates the majority of the cells in areas 18 and PMLS. In area PMLS, there is an additional eccentricity gradient: the proportion of monocular cells driven by the contralateral eye increases to about 20% beyond 10° of eccentricity (Hubel & Wiesel, 1969). Third, OD in area 21a favors the ipsilateral eye: About 50% of the cells respond more strongly to the ipsilateral eye's input while 30% of them prefer the contralateral eye (Dreher et al., 1993).

4.3. Putative mechanisms

Singer, von Grünau, and Rauschecker (1980) have described prolonged latencies and reduced response amplitudes of supragranular layers of striate cortex in response to stimulation of the amblyopic eye. They hypothesized that these might be caused by weaker intraareal transmission from layer IV to supragranular layers. Eschweiler and Rauschecker (1993) proposed that this reduced impact of the amblyopic eye might be due to disturbed synchronicity of excitatory inputs to the cortex.

In the primary visual cortex of cats strabismic amblyopia is associated with reduced response synchronization among neurons connected to the amblyopic eye (Roelfsema et al., 1994). This could account for the massive failure of neurons in area 21a to respond to stimulation of the amblyopic eye. Reduced synchrony has been shown both experimentally (Alonso, Usrey, & Reid, 1996) and in simulation studies (Lumer et al., 1997; Stevens & Zador, 1998) to impair transmission of activity from one processing stage to the next because it renders summation of synaptic potentials less effective. The reduced saliency of responses evoked from the amblyopic eye could have impaired responses in area 21a in two ways: First, through actual transmission failure of activity conveyed from area 17 to area 21a and, second, through activity-dependent long-term changes in synaptic efficacy. In the visual cortex, activity-dependent long-term modifications of synaptic efficacy follow Hebb's rule (Hebb, 1949). Synapses are strengthened if the probability is high that they are active in temporal contiguity with the postsynaptic target cell, but destabilize if they are inactive while their target is driven by other inputs (Miller, Keller, & Stryker, 1989; Rauschecker & Singer, 1979). Prior to squint induction, most cells in area 21a should have been binocular as in normal animals (Dreher et al., 1993) because the efferent projection cells in area 17 are binocular. Because of squint and resulting competition among afferents from the two eyes, cells in area 17 become monocular (Hubel & Wiesel, 1965a). This condition is, in turn, likely to lead to competition in area 21a among the afferents from area 17 that are now monocular. In this competition the afferents conveying activity from the amblyopic eye are likely to lose, because their activity is less
synchronized and will drive cells in area 21a less effectively than afferents representing the normal eye.

The amblyopia-related changes in OD were much less pronounced in area PMLS than in area 21a. One reason could be differences in the organization of subcortical inputs. Areas 18 and PMLS receive direct input from the LGN complex but area 21a does not (review: Orban, 1984). Moreover, the input to areas 18 and PMLS is mainly derived from Y-type retinal ganglion cells while input to area 21a is supplied predominantly by the X-system (Burke, Dreher, & Wang, 1998). We think that the difference in OD distributions is mainly due to the lack of direct input to area 21a because OD distributions in amblyopic cats are similar in all areas receiving direct LGN input, irrespective of whether this input is from the X-system (area 17) or the Y-system (area 18, PMLS).

It seems that area 21a is more sensitive to the loss of binocular congruency than area PMLS. This correlates well with area 21a being specialized for central vision by covering a strip between 10° above and 5° below the horizontal meridian (Dreher, Wang, Turlejski, Djavadian, & Burke, 1996). Moreover, cells in this area have small RFs which, in early development, might easily lead to a misalignment of the two monocular fields. In contrast, RFs of PMLS cells are distributed throughout the visual field and are significantly bigger than those of 21a cells at comparable eccentricities (Dreher et al., 1996).

4.4. Involvement of cortical pathways in amblyopia

It has been suggested that, in the cat, area 21a might be the gateway to a form-processing ventral stream while area PMLS could be regarded as the entrance to a distinct motion-processing dorsal stream (Burke et al., 1998; Dreher et al., 1996). Given the homologies between cat area PMLS and monkey area MT (Payne, 1993) as well as between cat area 21a and monkey areas VP and/or V4 (Dreher et al., 1993; Payne, 1993) our data predict that in amblyopic monkeys the weak eye should be less represented in areas VP and V4 than in area MT.

Psychophysical results suggest that the cortex is the neural site of amblyopia in humans (e.g. Hess & Pointer, 1985; Levi & Klein, 1985) and the nature of some of the deficits indicates anomalies in primary visual cortex. However, there is also evidence for deficits at higher levels of processing (Sharma, Levi, & Klein, 2000). Non-invasive imaging studies show that the relative reduction of responses to the amblyopic eye increases from striate to extrastriate areas (Anderson, Holliday, & Harding, 1999; Barnes, Hess, Dumoulin, Achman, & Pike, 2001; Goodyear, Nicolle, Humphrey, & Menon, 2000; Imamura et al., 1997; Muckli et al., 1998).

However, it is still unclear whether dorsal and ventral processing streams are affected differentially (Hess, Demanins, & Bex, 1997). The stronger deficit in the perception of color as compared to luminance stimuli (Mullen, Sankeralli, & Hess, 1996) suggests a stronger impairment of the ventral stream and measurements of contrast sensitivity indicated normal motion processing (Hess & Anderson, 1993; Hess, Howell, & Kitchin, 1978b). However, Wood and Kulikowski (1978) found motion and pattern vision to be equally affected and Rentschler, Hilz, and Brettel (1981) came to the same conclusion, studying apparent motion. Impaired
motion processing is also suggested by the observations that the velocity of gratings moving in temporal direction is underestimated (Tychsen & Lisberger, 1986) and that motion aftereffects are weaker in amblyopes (Hess et al., 1997). Thus, psychophysical data suggest impairment of functions attributed to both dorsal and ventral pathways.

Measurements of cortical evoked potentials in amblyopic children (Kubova, Kuba, Juran, & Blakemore, 1996) revealed a reduced amplitude and prolonged latency of responses to pattern reversal whereas motion onset responses were not affected suggesting a relative sparing of the dorsal pathway. This result is in line with imaging data (fMRI; Muckli et al., 1998) which suggests that activation deficits in prestriate visual areas are more pronounced along the temporal pathway from area VP to the fusiform gyrus than along the dorsal pathway from V2 to posterior intraparietal areas. Thus, in agreement with the present study, measurements of neuronal activity favor the view that the ventral pathway is more affected in amblyopia than the dorsal pathway.

Acknowledgements
We like to thank Ruxandra Sireteanu for her collaboration in the behavioral testing of the cats. We are grateful also to Carmen Selignow, Petra Janson, Hanka Klon-Lipok, Sandra Schwegmann, and Maren Kurschat for excellent technical assistance, and to Renate Ruhl and Selina Völzing for their help in preparing the figures. Supported by the Heisenberg Program of the DFG, the Minna-James-Heineman Foundation and the Max Planck Society.

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