Effects of Pattern Deprivation on Visual Cortical Cells in the Rabbit: A Reevaluation

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SUMMARY AND CONCLUSIONS

1. The response properties of 217 cells recorded from the monocular segment of primary visual cortex in rabbits reared with lid suture of the contralateral eye (monocular deprivation, MD) were studied. These data were compared with 280 cells recorded from normal rabbits.

2. There was no change in the percentage of orientation-selective cells, nonorientation-selective cells, or unmappable/unresponsive cells in MD animals compared with normals.

3. Among orientation-selective cells the orientation-tuning range of cells in MD animals was normal, and the predominance of cells with horizontal preferred orientation was maintained. However, some abnormalities were seen in orientation-selective cells of MD animals. These included 1) an increased frequency of SI cells; 2) a change in the distribution of preferred orientations; 3) a disruption of the clustered organization of the cortex; 4) a decrease in direction selectivity; 5) an increase in the percentage of cells preferring slow stimulus movements and having low spontaneous activity; 6) an increase in receptive-field size in all cell classes except SI.

4. Among nonorientation-selective cells there was an increase in the percentage of movement sensitive cells and an increase in receptive-field size in MD animals.

5. It is concluded that the effects of MD are much less severe in rabbit than in cat. In MD rabbits, many cells develop normally. In cells that do not develop normally, many of the changes observed can be interpreted as reflecting deficits in inhibitory functions.

INTRODUCTION

The visual system of the rabbit is quite immature at the time of birth (for review, see Ref. 35). Even at the time of eye opening (11 days postnatal), visual cortical neurons have immature receptive-field characteristics, and the acquisition of mature receptive-field characteristics occurs during a period extending at least through the first postnatal month (29). The rabbit geniculostriate system, therefore, would appear to offer an ideal system for the study of developmental processes. However, previous investigations of the effects of selective (30) or nonselective (12, 13, 21) deprivation of patterned visual experience during development suggest that the rabbit, unlike the cat, is relatively immune to the effects of early deprivation (for review of cat literature, see Ref. 47). Chow and his co-workers (12, 13) have reported that monocular deprivation (MD) by lid suture merely delays the development of cortical receptive fields in the rabbit, and that by the age of three months the visual cortex of the lid-sutured rabbit has achieved normal mature function. They suggest that the ineffectiveness of monocular suture in disrupting rabbit visual cortical organization can be attributed to the relative absence of binocular competitive interactions in the rabbit's visual system.

Several factors dictated the need to reexamine the effects of lid suture on development of the rabbit visual cortex. First, recent evidence indicates that, in the cat, deprivation per se has consequences that are measurable and independent of factors involving binocular competition; these studies have involved recording from the monocular segment of visual cortex in monocularly deprived cats, or recording from the binocular segment of visual cortex in binocularly deprived cats (60, 62). Second, previous work from this laboratory has shown that the rabbit visual cortex contains a much higher percentage of orientation-selective cells and a much lower per-
centage of unresponsive cells with indefinite response characteristics than had been previously reported (35). This finding of a more significant representation of orientation selectivity in rabbit visual cortex necessitated a reevaluation of the effects of lid suture on these orientation-selective cells; in cat and monkey visual cortex, most cells are orientation selective, and it is these cells that are susceptible to early deprivation. Third, it has been recently demonstrated that the functional organization of the rabbit visual cortex can, in fact, be modified by manipulation of early experience. Direction selectivity of orientation selective cells is dramatically reduced in the visual cortex of rabbits deprived of experience of visual movement during development (39, 40, 41). Previously studies of MD rabbit did not document the presence or absence of direction selectivity in orientation-selective cells. The present study, therefore, investigated whether deprivation of experience of visual patterns, like deprivation of experience of visual motion, disrupts the organization of direction selectivity in rabbit visual cortex.

METHODS

Subjects

Control recordings were obtained from normal Dutch-belted rabbits aged 2–6 mo. Some were obtained from a dealer and some were born and raised in the laboratory. Some of these data have been described previously (35). However, additional control data were obtained during and after the time period during which the experimental data were recorded, and did not differ significantly from the control data recorded previously. Experimental data were obtained from Dutch-belted rabbits aged 2–5 mo which had the right eyelid sutured prior to the time of natural eye opening (which occurs at age 10–11 days postnatal). These animals were either born in the laboratory or the litters, with the mother, were obtained from a dealer when the pups were 5–7 days old. In agreement with previous studies (10, 11, 19, 27, 31, 32, 34) no differences were observed between rabbits aged 2 mo and the older rabbits for either normal or experimental conditions.

Suture

Lid suture was performed in pups prior to the time of natural eye opening, under halothane (Fluothane) anesthesia in 50% N₂O-50% O₂. The lid margins of the right eye were cut and sutured. An ophthalmic antibiotic ointment (Neosporin) was applied to the cornea and lids, and an intramuscular injection of a broad-band antibiotic (Bicillin) was given. Animals were inspected daily for infection or openings of the eyelid. Peepholes that occasionally developed were resutured immediately. This occurred in only two animals. Animals that developed larger lid openings were discarded.

Physiological recording

When animals were 2–6 mo of age, preparation for recording was carried out. Under barbiturate anesthesia (Nembutal, 35 mg/kg), supplemented by topical application of local anesthetic (Novocaine, 1–2 mg) in the area of the incision, the skin was incised, the skull overlying striate cortex was thinned with an electric burr, and a headbolt was cemented to the skull such that the animal could be held in the stereotaxic frame without the use of ear bars or pressure points, and without obstruction of the visual field. The incision was closed with wound clips. On the day of recording, 2–7 days after the preparation, the scalp incision was reopened under halothane anesthesia and infused with local anesthetic. A tracheotomy was performed. The animal was then held by the head bolt, paralyzed with Flaxedil, (10 mg iv), and respirated. A Beckman analyzer was used to monitor expired CO₂ throughout the experiment, and the respirator was adjusted to maintain a level of 3.5–4.0%. Paralysis was maintained with a constant infusion of Flaxedil (10 mg/hr im), anesthesia was maintained with an initial dose of Nembutal (30 mg/kg) and supplemental doses at regular intervals. The sutured eye was then opened, pupils were dilated with local application of atropine, the corneas protected with a contact lens, and the eye focused on a tangent screen 5 cm from the right eye.

The remaining thin layer of bone was removed, and a glass-coated platinum-iridium electrode was lowered, by a hydraulic microdrive, through dura to the cortical surface. The electrode was angled at least 30° to increase the cortical area sampled in one penetration and to permit recording across clusters or columns. In some animals, the electrode was advanced at least 75 pm between units to reduce sampling bias. There was no significant difference between data obtained from these animals and from animals in which this control was not used. There was also no significant difference in the mean distance between recorded units for the two groups of animals which was 89 ± 44 μm in control animals and 94 ± 30 in experimental animals.

Recordings were made from the monocular segment of the left primary visual cortex from units with biphasic waveforms with a duration of >1 ms. Occasionally, recordings were made from

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units with waveforms which were monophasic, positive, had a duration of <0.5 ms. These were assumed to be lateral geniculate axons and were not studied. Most cells were recorded within the area of the representation of the visual streak to reduce variability in our sample. However, there are no cortical landmarks in the rabbit's lissencephalic brain, and some recordings were made from more peripheral areas of the visual-field representation (see RESULTS). These data are included in all analyses except determination of receptive-field location (35).

Visual stimulation

During the initial determination of each cell's receptive-field characteristics, stimuli were presented manually on the screen, using a tripod-mounted projector with a bivariable slit. Stimuli consisted of bars, slits, and spots, moving or flashing, with an average illumination of 1.2 log units above background. The receptive-field size and location was then recorded on a sheet of tracing paper attached to the screen onto which the optic disk was also back reflected and drawn. Subsequently, automated presentation of moving or flashing stimuli was used, in combination with a poststimulus time histogram analyzer (Ortec), or a spike counter (Hewlett-Packard), to obtain quantitative measures of the cell's response properties. Not all response parameters were studied quantitatively in every cell but some quantitative analysis was made on ~90% of cells recorded. Velocity sensitivity was assessed quantitatively in all cells that responded to moving stimuli. Direction selectivity was assessed quantitatively in all cells in which the presence or absence of direction selectivity was not obvious from listening to the audio monitor. Adaptation and response to stroboscopic stimuli were assessed quantitatively in at least 50% of cells.

Characterization of response properties

RECEPTIVE-FIELD SIZE. Receptive-field borders were determined by using the method outlined by Barlow et al. (2) but were mapped for only one eye since recordings were made only from monocular cortex. Receptive-field area was measured in square centimeters, and data on receptive-field sizes and positions are given as measured directly from the tangent screen. The use of tangent screen plotting of receptive fields produces an overestimate of distance. However our calculations (4) and those of Bishop, Kozak, and Vakkur (5) indicate that the difference between measurements on a tangent screen 57 cm from cat's eye and measurements on a hemisphere are 0.7° (3.5%) at an angle of 20°. The average eccentricity of receptive fields recorded in this study is only 12°, and modifications in receptive-field size could not be accounted for by this factor (see RESULTS). The receptive-field size was defined as the largest area in which a visual stimulus elicited a response.

VELOCITY. The preferred velocity was determined by using several presentations of the optimal stimulus at velocities of 1 to 100°/s. The peak discharge rate was used to determine the preferred velocity, which was then classified as slow (1-5°/s), medium (5-15°/s), fast (>15°/s), or broad (responding equally well to all velocities). This characteristic was determined quantitatively in all cells tested.

ADAPTATION. A cell was classified as showing adaptation if three successive presentations of the optimal stimulus, at an interstimulus interval of 1 to 2 s, resulted in a substantial decrement in the response to the third stimulus which could be audibly detected by two observers or was quantified as being at least 50% less than the response to the first stimulus.

SPONTANEOUS ACTIVITY. The mean spontaneous activity was assessed from 3 successive samples of 10 s during which no visual stimuli were presented. The activity level was then classified as low (0-5 spikes/10 s), medium (5-20 spikes/10 s), or high (>20 spikes/10 s).

RESPONSE TO STROBOSCOPIC STIMULATION. The effect of stroboscopic stimulation was tested in two ways. First, the cell's response to a stroboscopic stimulus was assessed. The strobe light (flash duration: 9 μs) was presented at rates of 1 to 20 Hz. If the cell responded, the optimum rate was noted. Cells usually responded with one spike/stimulus at the optimal rate. At nonoptimal rates, following was incomplete, and not every stimulus evoked a response. Second, the effect of background stroboscopic illumination was assessed by presenting the optimal stimulus against a background of 16-Hz flashes. The cell's response (spikes/stimulus) was classified as being facilitated, inhibited or unaffected by background stroboscopic illumination. Every condition was tested at least three times to determine the reliability of these changes.

Receptive-field classification: orientation selectivity

Initially, each cell was classified into one of two classes: orientation selective or nonorientation selective. Cells which were orientation selective were distinguished from cells which were purely uni- or bidirectionally selective by criteria described by Pettigrew (42). A cell was tested to determine if 1) moving spots were less effective than moving lines, or 2) a line flashed in the preferred orientation was more effective than a line flashed in the orthogonal orientation. No cell was classified as orientation selective unless it responded preferen-
tially to the flashed line in the preferred orientation. Of these, approximately 70% also responded more strongly to moving lines than spots.

CLASSIFICATION OF ORIENTATION SELECTIVE CELLS. Each cell was classified as simple type I (SI), simple type II (SII), or complex. In addition, each cell was subclassified as hypercomplex if the receptive field was end stopped. SI cells had only one excitatory region, which was responsive either to the onset or to the offset of light, and/or responded either to the leading or to the trailing edge of a moving bar. SII cells had two adjacent, antagonistic regions of the receptive field, one being responsive to the onset of light and/or to leading edges, the other being responsive to the offset of light and/or to trailing edges of a moving light bar. The distinction between SI and SII cells has been used by others (45, 54). It has been shown that, in rabbits, SII cells tend to predominate in lamina IV and that SII cells also differ from SI cells also in their developmental properties (35, 36). In addition, SI cells are encountered more frequently in rabbits than in cats, and represent a significant population of rabbit visual cortical cells. Complex cells did not have spatially separable on and off regions, and responded to an optimally oriented stimulus moving anywhere within the receptive field.

For all orientation-selective cells, the following response characteristics were determined: 1) Orientation-Tuning Range And Preferred Orientation. The tuning range was determined by presenting stimuli at the optimum velocity through all orientations, and measuring the angle over which an oriented stimulus elicited a response above the background spontaneous level. The preferred orientation of the cell was then taken as the midpoint of this tuning range (56). 2) Direction Selectivity. Orientation-selective cells were classified as direction selective if movement of the bar in the preferred direction elicited twice as many spikes as movement in the opposite direction.

CLASSIFICATION OF NONORIENTATION-SELECTIVE CELLS. Cells were classified into the following receptive-field classes: 1) Concentric cells had a center area that responded to the onset or offset of light and a concentric antagonistic surround. 2) Uniform cells responded either to the leading or to the trailing edge of a moving bar. SII cells had two adjacent, antagonistic regions of the receptive field, one excitatory region, which was responsive either to the onset or to the offset of light, and/or responded inconsistently to changes in illumination, but the borders of their receptive fields could not be determined. None showed orientation or direction selectivity. For all these nonorientation-selective cells, the presence or absence of internal inhibition, internal summation, and surround inhibition was determined. A cell was classified as showing internal inhibition when the optimal response was elicited by presentation of a stimulus smaller than the receptive-field size. A cell was classified as showing internal summation when the response increased with increasing stimulus size, and as showing surround inhibition when stimulation of the area surrounding the excitatory receptive field reduced the response to the optimal stimulus within the receptive field.

Laminar localization

During the electrode penetration, the depth relative to the cortical surface of each recorded cell was noted. At the end of the penetration, lesions were made in at least two locations (5 μA for 1–5 s). Animals were then killed with an overdose of Nembutal, perfused with saline followed by 10% formal saline, and the brains were cut and processed for localization of these lesions. These lesions were then used to determine the laminar position of recorded cells.

Data analysis

We have previously noted that cortex is easily depressed in rabbits and have suggested that the percentage of indefinite cells is increased in nonoptimal preparations. In both our normal and MD samples, therefore, data were discarded from animals in which more than 30% of cells were indefinite and fewer than seven cells were recorded in one penetration through striate cortex. Such criteria for an optimal preparation would, of course, be unacceptable if the lid suture increased the percentage of indefinite, or unresponsive cells. However, the frequency of encounter of nonoptimal preparations, as defined by these criteria, did not differ from normal and MD animals. Using these criteria, of the normal animals, recordings were made from 31 rabbits, and 6 were discarded as nonoptimal. Of the MD rabbits, recordings were made from 28 rabbits, and 4 were discarded. We recorded an average of 11.1 cells from the 25 normal rabbits included in this study, and an
average of 10.8 cells in the 24 MD animals included in this study. Only one penetration was made through cortex in each animal because the rabbit cortex tends to deteriorate rapidly after one penetration has been made and electrolytic lesions used to mark the recording site. Since within-animal samples are therefore necessarily small, data were pooled within the normal and MD groups for statistical analysis. Our major findings (see RESULTS) of changes in receptive-field size and direction selectivity in MD animals were observed in every MD animal. The $\chi^2$ and $t$ tests were used to assess statistical significance of results obtained.

RESULTS

Receptive-field classification

A total of 280 cells was recorded from normal animals and 217 from MD animals. Every cell recorded was classified into one of the receptive-field types described above, and these data are shown in Table 1.

Comparison of the relative frequency of occurrence of each receptive-field type in normal and MD animals reveals that the overall percentage of orientation-selective cells is not changed by monocular suture; 61% of cells recorded in normal animals and 60% of cells recorded in MD animals were orientation selective. However, the distribution of receptive-field types within these two major subgroups does show significant changes. Within the group of orientation selective cells, SI cells are recorded more frequently in MD than in normal animals (MD 30.4%; normal 17.1%); all other types of orientation-selective receptive fields are recorded less frequently in MD than in normal animals. Within the group of nonorientation-selective cells the distribution of receptive-fields types is also altered; movement-sensitive cells are encountered more often in MD animals than in normal animal (MD 24.8%; normal 16.1%), whereas all other nonorientation-selective cells are encountered less often in MD than in normal rabbits. There is no difference between MD and normal rabbits in the frequency of encounter of indefinite and unresponsive cells. A $\chi^2$ test was used to compare the frequency of occurrence of each type of receptive field in MD and normals; the differences were significant ($\chi^2 = 40.9; \text{df} = 10; P < 0.001$).

ORIENTATION-SELECTIVE CELLS.

Distribution of preferred orientations. Figure 1 shows the preferred orientation of all orientation-selective cells in normal and MD rabbits. In the normal rabbits we confirmed the previous finding that, in the distribution of preferred orientations, a distinct peak occurs around the horizontal orientation and a smaller peak around the vertical orientations. In MD animals, the peak around the horizontal orientation is much less distinct, and there is no evidence of a peak for vertical preferred orientations. A $\chi^2$ analysis comparing the representation of each preferred orientation showed a significant difference between normal and MD rabbits in this distribution ($\chi^2 = 36.5; \text{df} = 17; P < 0.01$). Since orientation tuning is fairly broad in rabbits compared with cats (33), and since the eye position cannot be determined in rabbits with the same accuracy possible in cats, it is possible that the existence of peaks in orientation preference might be masked by these factors. To examine this, we assigned cells, by preferred orientation, into three broad categories: horizontal $\pm 30^\circ$, vertical $\pm 30^\circ$, and oblique. If all orientations are equally represented, then the percentage of cells in each of these categories should not differ. Table 2 shows the percentage of orientation selective cells which fall into each of these categories.

<table>
<thead>
<tr>
<th></th>
<th>SI</th>
<th>SI-II</th>
<th>SI</th>
<th>SI-II</th>
<th>Complex</th>
<th>Complex-H</th>
<th>Centric</th>
<th>Direction</th>
<th>Uniform</th>
<th>Movement</th>
<th>Indefinite</th>
<th>Unresponsive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>48</td>
<td>18</td>
<td>51</td>
<td>6</td>
<td>40</td>
<td>14.3</td>
<td>20</td>
<td>7</td>
<td>2</td>
<td>10</td>
<td>45</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>(17.1)</td>
<td>(6.4)</td>
<td>(18.2)</td>
<td>(2.1)</td>
<td>(14.3)</td>
<td></td>
<td>(7.1)</td>
<td>(3.5)</td>
<td>(0.7)</td>
<td>(10.1)</td>
<td>(16.1)</td>
<td>(11.1)</td>
</tr>
<tr>
<td>MD</td>
<td>66</td>
<td>7</td>
<td>35</td>
<td>0</td>
<td>5</td>
<td>8.3</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>54</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>(30.4)</td>
<td>(3.2)</td>
<td>(16.1)</td>
<td>(0.0)</td>
<td>(8.3)</td>
<td></td>
<td>(0.9)</td>
<td>(0.4)</td>
<td>(0.9)</td>
<td>(10.1)</td>
<td>(24.8)</td>
<td>(10.1)</td>
</tr>
</tbody>
</table>

SI, simple type I; SI, simple type II; H, hypercomplex.
In MD animals, 47% of cells prefer an orientation within 30° of horizontal. These data suggest that although the orientation preference distribution in MD rabbits is highly distorted, the predominance of horizontal preferences, observed in normals may be less disrupted, in MD animals, than the peak for vertical orientations.

Columnar or cluster organization of orientation preference. It has been previously demonstrated that in the normal rabbit, orientation preferences are organized not in the precise columnar organization observed in cat but in clusters (7, 33). This finding has been confirmed by Bousfield (9). If units with similar orientation preferences tend to occur in clusters, then the change in orientation preference between unit pairs recorded in close proximity will be less than the change in orientation preference between unit pairs recorded at a greater interunit distance. We measured the change in preferred orientation for pairs of units recorded within 200 µm in the course of an electrode penetration. Figure 2 shows these data for normal and for MD animals. There is a clear loss in MD animals of the clustering effect observed in normals, as demonstrated by the peak, in the normal data, of adjacent pairs of cells with an orientation change < 10° (χ² = 27.64; df = 8; P < 0.001).

There are several possible interpretations of this finding. One possibility is that the orientation-tuning range is broader in MD than in normal animals, and that therefore the clustering effect is masked. To investigate this hypothesis, the orientation-tuning range of cells in MD rabbits was measured.

Orientation-tuning range. Figure 3 shows the average orientation-tuning range for each type of orientation-selective cell in normal and MD rabbits. The mean orientation-tuning range is somewhat higher for MD animals

<table>
<thead>
<tr>
<th></th>
<th>Horizontal ±30°</th>
<th>Vertical ±30°</th>
<th>Oblique</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>41.5</td>
<td>39.5</td>
<td>19.0</td>
</tr>
<tr>
<td>MD</td>
<td>47.6</td>
<td>26.9</td>
<td>25.4</td>
</tr>
</tbody>
</table>

FIG. 1. Histogram showing the preferred orientation of all orientation-selective cells recorded. Horizontal is represented at 0° and 180°; vertical is represented at 90°.
than for normal animals in all classes of orientation-selective cells. However, these differences do not reach significance (SI: $t = 1.59$, $df = 1,129$, NS; SII: $t = 0.40$, $df = 1.85$, NS; complex: $t = 1.17$, $df = 1.62$, NS). Thus, in the organization of orientation selectivity, those cells recorded in MD animals appeared in most respects indistinguishable from those recorded in normals. Responses of two typically vigorously responsive cells recorded in MD rabbits are shown in Fig. 4.

*Direction selectivity.* In normal rabbits, virtually all orientation-selective cells (87%) are also direction selective. In contrast, in MD animals, only 66% are direction selective. To determine whether this decrease in direction selectivity in MD animals occurred uniformly, or was restricted to specific directions, the number of cells preferring each possible direction was calculated. These data are shown in Table 3.

In normals, as discussed above, preferred orientations peak at horizontal and vertical. Therefore, one would expect peaks in the preferred directions at 90° (movement towards superior visual field), and 270° (towards inferior visual field) for the horizontally oriented fields, and peaks at 0° (towards posterior visual field) and 180° (towards anterior visual field) for cells with vertical orientation preferences. These peaks are clearly visible in the normal data, and there is no evidence of a selective preference for one of the two possible direction preferences for each orientation; for example, horizontally oriented receptive cells are equally likely to prefer movement towards the superior or the inferior visual field. In MD animals, the sample of direction-selective orientation-selective cells is much smaller. However, as shown in Table 3, the loss occurs in all possible directions and is not selective for any specific directions.

We were also interested in determining whether the decreased direction sensitivity of
FIG. 4. Two cells that were both orientation selective and direction selective, recorded in MD rabbits. Length of each arrow represents number of spikes elicited by movement of stimulus in the direction of arrow. Cell on left is very finely tuned. Dotted circle represents mean spontaneous activity. Movement of the stimulus in directions other than the preferred direction inhibited spontaneous activity. Cell on right is more broadly tuned and has no spontaneous activity.

orientation-selective cells, observed in MD rabbits, was observed uniformly across all receptive-field classes or whether it was selective for a specific type of cell. The percentage of direction selective or nondirection-selective cells for each of the classes of orientation-selective receptive fields in normal and MD animals was therefore calculated. These data are shown in Fig. 5. Although the decrease in direction selectivity in MD animals is relatively small in all receptive-field classes, the loss is least in cells with complex receptive fields and greatest in SII cells.

NONORIENTATION-SELECTIVE CELLS. As described above, there is a significant increase in the frequency of encounter of cells with movement-sensitive receptive fields in MD animals. To determine whether the response characteristics of these movement-sensitive cells differed from those encountered in normal animals, and to assess the integrity of inhibitory mechanisms in these cells, the number of cells showing internal inhibition or surround inhibition was counted. These

TABLE 3. Preferred direction of cells

<table>
<thead>
<tr>
<th>Preferred Direction</th>
<th>Normal</th>
<th>MD</th>
</tr>
</thead>
<tbody>
<tr>
<td>±15°</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–30</td>
<td>16 (10.8)</td>
<td>2 (2.5)</td>
</tr>
<tr>
<td>30–60</td>
<td>8 (5.4)</td>
<td>4 (5.1)</td>
</tr>
<tr>
<td>60–90</td>
<td>11 (7.4)</td>
<td>9 (11.4)</td>
</tr>
<tr>
<td>90–120</td>
<td>26 (17.6)</td>
<td>6 (7.5)</td>
</tr>
<tr>
<td>120–150</td>
<td>6 (4.1)</td>
<td>5 (6.3)</td>
</tr>
<tr>
<td>150–180</td>
<td>14 (9.5)</td>
<td>10 (12.6)</td>
</tr>
<tr>
<td>180–210</td>
<td>12 (8.1)</td>
<td>4 (5.1)</td>
</tr>
<tr>
<td>210–240</td>
<td>3 (2.0)</td>
<td>5 (6.3)</td>
</tr>
<tr>
<td>240–270</td>
<td>10 (6.7)</td>
<td>13 (16.5)</td>
</tr>
<tr>
<td>270–300</td>
<td>20 (13.5)</td>
<td>9 (11.4)</td>
</tr>
<tr>
<td>300–330</td>
<td>7 (4.7)</td>
<td>6 (7.5)</td>
</tr>
<tr>
<td>330–360</td>
<td>15 (10.1)</td>
<td>6 (7.5)</td>
</tr>
</tbody>
</table>

Numbers and percentages (in parentheses) of cells recorded that preferred each possible direction of stimulus movement (±15°). See text for visual field representation.

FIG. 5. Percent of orientation-selective cells in each receptive-field class that were also direction selective.
TABLE 4. Types of inhibition

<table>
<thead>
<tr>
<th></th>
<th>Surround Inhibition</th>
<th>Internal Inhibition</th>
<th>No Inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>18 (48)</td>
<td>2 (5)</td>
<td>18 (47)</td>
</tr>
<tr>
<td>MD</td>
<td>17 (32)</td>
<td>8 (15)</td>
<td>28 (53)</td>
</tr>
</tbody>
</table>

Numbers and percentages (parentheses) of movement-sensitive cells showing surround inhibition or internal inhibition.

data are shown in Table 4. There was no significant difference between normal and MD rabbits ($\chi^2 = 3.2; \text{df} = 2; \text{NS}$)

ALL RECEPTIVE-FIELD CLASSES.

Receptive-field size. The mean receptive-field size in MD animals was significantly larger than in normal animals. This could not be accounted for by receptive-field location since the mean distance of the receptive fields from the center of the visual streak was equivalent (normals $13^\circ$, MD $11.1^\circ$). To determine whether this change in the mean receptive-field size in MD animals reflected a shift in the overall distribution of receptive-field sizes or a change in some specific sample of cells in the cell size distribution, the number of cells in each receptive-field size was calculated. Histograms of the receptive-field size distributions are shown in Fig. 6. Inspection of Fig. 6 shows that although there are cells in MD rabbits that are as small as the smallest seen in normal animals, there is an increase in the percentage of cells that have receptive fields larger than 20 cm$^2$. In normal animals 43% of cells have receptive fields $\geq$ 20 cm$^2$, whereas in MD animals this percentage is increased to 63.1%. These distributions are significantly different ($\chi^2 = 28.82; \text{df} = 10; P < 0.01$). To determine whether this increase in the receptive-field size was occurring uniformly or was selective for specific cell types, the receptive-field size for each receptive-field class was calculated, and these data are shown in Fig. 7.

The SI cells, which are well represented in the population of cells recorded are also not significantly different in receptive field size in MD animals. However, SII, complex, and nonoriented cells all show a dramatic and significant increase in mean receptive-field area. (SI: $t = 0.7, \text{df} = 1,134, \text{NS}$; SII: $t = 3.8, \text{df} = 1,91, P < 0.001$; complex: $t = 30, \text{df} = 1,64, P < 0.001$; nonoriented: $t = 2.1, \text{df} = 1,142, P < 0.001$). Optical problems could not be a factor in these results since the receptive-field area of the SI cells in these animals is normal.

Velocity selectivity. Velocity preferences of cells recorded are shown in Table 5. In normal animals, for all types of receptive field, approximately equal percentages of cells prefer slow or medium velocities. For all oriented receptive-field classes, very few cells prefer fast movement or respond equally well to all velocities, whereas for nonoriented

![Fig. 6. Histogram of receptive-field area of all cells recorded.](http://jn.physiology.org/)

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receptive-field classes, fast and broad velocity preferences are frequently observed in addition to slow or medium velocity preferences. A major difference in MD animals is the relative increase in the percentage of cells preferring slow velocities and the relative decrease in cells preferring medium velocities. In MD animals, also, more complex cells respond to fast or broad ranges of velocities than is observed in normals. These differences between normal and MD animals are significant ($\chi^2 = 14.2$, $df = 3$, $P < 0.001$).

**Spontaneous activity.** Mean spontaneous activity of cells recorded is shown in Table 6. Nonoriented cells, in both MD and normal rabbits, are about as likely to have low, medium, or high spontaneous activity. For cells with oriented receptive fields, however, there is a clear difference between MD and normal animals, with many more MD-oriented cells (83%) having low spontaneous activity than did normal cells (56%), and a corresponding decrease in MD oriented cells with medium spontaneous activity (11%) compared with normal cells (35%). These differences are significant ($\chi^2 = 24.2$, $df = 2$, $P < 0.001$).

**Adaptation.** There was no significant difference between normal and MD animals in the percentage of cells showing adaptation. These data are shown in Table 7.

**Laminar analysis.** For those cells for which histological reconstruction of the electrode tract permitted accurate laminar localization, analyses were carried out to compare normal and MD animals on all of the response characteristics described above. Cells were classified as being in supragranular layers, infragranular layers, or in lamina IV. The

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**TABLE 5. Velocity preferences of cells recorded**

<table>
<thead>
<tr>
<th></th>
<th>Slow</th>
<th>Medium</th>
<th>Fast</th>
<th>Broad</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simple I</td>
<td>23 (41.8)</td>
<td>27 (49.1)</td>
<td>2 (3.6)</td>
<td>3 (5.5)</td>
</tr>
<tr>
<td>Simple II</td>
<td>22 (44.9)</td>
<td>24 (48.9)</td>
<td>1 (2.0)</td>
<td>2 (4.1)</td>
</tr>
<tr>
<td>Complex</td>
<td>18 (43.9)</td>
<td>19 (46.3)</td>
<td>3 (7.3)</td>
<td>1 (2.4)</td>
</tr>
<tr>
<td>Nonoriented</td>
<td>12 (22.2)</td>
<td>14 (25.9)</td>
<td>13 (24.1)</td>
<td>15 (27.7)</td>
</tr>
<tr>
<td>MD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simple I</td>
<td>47 (64.8)</td>
<td>18 (24.7)</td>
<td>6 (8.2)</td>
<td>2 (2.7)</td>
</tr>
<tr>
<td>Simple II</td>
<td>20 (52.6)</td>
<td>15 (39.5)</td>
<td>1 (2.6)</td>
<td>2 (5.2)</td>
</tr>
<tr>
<td>Complex</td>
<td>11 (47.8)</td>
<td>5 (21.7)</td>
<td>3 (13.0)</td>
<td>4 (17.4)</td>
</tr>
<tr>
<td>Nonoriented</td>
<td>22 (38.6)</td>
<td>9 (15.8)</td>
<td>13 (22.8)</td>
<td>13 (22.8)</td>
</tr>
</tbody>
</table>

Number and percentages (in parentheses) of cells preferring slow, medium, or fast stimulus movement or responding equally well to all velocities (broad). See METHODS for range of velocities included in each category.

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**TABLE 6. Mean spontaneous activity of cells recorded**

<table>
<thead>
<tr>
<th></th>
<th>Low</th>
<th>Medium</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orientation selective</td>
<td>88 (5.6)</td>
<td>54 (34.8)</td>
<td>13 (8.3)</td>
</tr>
<tr>
<td>Nonorientation selective</td>
<td>94 (37.0)</td>
<td>36 (40.1)</td>
<td>74 (67.0)</td>
</tr>
<tr>
<td>MD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orientation selective</td>
<td>109 (83.3)</td>
<td>15 (11.3)</td>
<td>7 (5.4)</td>
</tr>
<tr>
<td>Nonorientation selective</td>
<td>29 (39.2)</td>
<td>23 (31.1)</td>
<td>22 (29.7)</td>
</tr>
</tbody>
</table>

Number and percentages (in parentheses) of cells with low, medium, or high spontaneous activity. See METHODS for range included in each category.

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**TABLE 7. Number and percentages (in parentheses) of cells showing response decrement to repeated stimulation**

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th></th>
<th>MD</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Orientation selective</td>
<td>39 (35)</td>
<td>19 (40)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonorientation selective</td>
<td>38 (30)</td>
<td>16 (29)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
differences observed between normal and MD animals were not restricted to any specific laminar localization, and the laminar organization previously described in normals (33) was confirmed.

**Subpopulations of cells in MD.** The major effects of MD were the increased receptive-field size and the loss of DS in some of the orientation-selective cells. I hypothesized that those cells that maintained DS in the absence of normal early visual experience might differ from those that did not, and so I compared direction-selective/oriented cells with nondirection-selective/oriented cells recorded in MD animals. No differences were found between the two populations in their orientation preferences, orientation range, velocity preferences, adaptation, or receptive-field size.

**DISCUSSION**

**Other studies of MD rabbits**

Previous studies by Chow and co-workers (12, 13) have reported that, despite delay in development, normal functional organization of receptive fields is observed in MD rabbits aged 3–14 mo. In these studies, the analysis of cortical function was limited to a classification of receptive-field types. To this extent, the present findings effectively confirm those studies. I observed no differences between normal and MD rabbits in the percentages of cells that are orientation selective, non-orientation selective, and unresponsive. The other findings of the present study cannot be compared with those of Chow et al. because the results involve subclassifications of receptive-field types or other response parameters which they did not describe.

**Orientation-selective cells**

**ORIENTATION SELECTIVITY.** Orientation selectivity appears to be relatively unaffected by pattern deprivation in the rabbit. The percentage of cells that are orientation selective is unchanged in MD rabbits, and orientation-selective cells have receptive fields that are normal in most respects. The orientation-tuning range is normal, and the cells do not show any change in fatigability.

However, I did observe some abnormalities in the organization of orientation selectivity. One of these was the disruption of the clustered organization of cells with similar preferred orientations. We have suggested previously (35) that this cluster type of organization observed in rabbit visual cortex is less precise than the columnar organization of orientation preferences observed in cats, and that this less-precise type of organization of orientation selectivity is characteristic of mammals in which a substantial proportion of visual cortical cells are not orientation selective. However, this study shows that, in MD rabbits, this relatively imprecise cluster organization is further disrupted. This suggests that most cortical cells may initially have a broad range of potential preferred orientations, and that visual experience imposes a restriction, within the framework of a clustering pattern, on this broad range. Such a developmental mechanism could also underlie another abnormality of orientation selectivity described above: the decreased frequency of cells preferring vertical orientations.

The high frequency of cells preferring a horizontal orientation is, however, maintained in MD rabbits. This suggests that cells with horizontal preferred orientations have a pre-specified orientation preference, independent of experience, but that other cells may be influenced by visual experience in the final determination of their preferred orientation. There is evidence that both the distribution of preferred orientation and the organization of orientation within columns are subject to modification by early deprivation in cats (6, 22), as in rabbits. Hirsch and colleagues have reported that horizontal and vertical preferred orientations are represented in cat visual cortex independent of experience of orientation, whereas oblique orientations are experience dependent (28). However, in cats deprived of all pattern experience many cells are unresponsive to any orientation, and Rauschecker and Singer (44) suggest that visual experience serves both to maintain innate properties and to specify innately unspecific neurons. This point will be discussed further, but it appears that, in both cat and rabbit, the distribution of preferred orientations may be modified by visual experience, and that cells with a horizontal preferred orientation are least dependent on visual experience for their development or maintenance.

There is conflicting evidence on the effects of deprivation on the columnar organization of orientation preferences in cats. In stripe-reared cats, data of Stryker et al. (55) suggest
that columnar organization of orientation selectivity is maintained, with some unresponsive areas reflecting cells which never experience their preferred orientation. However, Blakemore's data (6) suggest that the preferred orientation of cells is modified by experience. His data, and those of Singer et al. (52) indicate a disruption of normal columnar organization of orientation. In the more directly comparable study of cats reared with pattern deprivation, Watkins et al. (60) report that successive cells tended to have similar stimulus requirements, but no quantitative data are given on changes in preferred orientation between adjacent cells.

We have preliminary evidence (36) that the clustered organization of orientation preferences seen in MD rabbits is similar to that observed in immature rabbits. This would suggest that visual experience plays a role in the development, rather than the maintenance, of the clustered organization of orientation preferences. Such development could involve postnatal development of intracortical inhibitory mechanisms, or it could involve the selective loss of "exuberant" excitatory connections. The decrease in dendritic spine density that occurs in rabbit visual cortical neurons during the first two postnatal months could play a role in this process (37).

FREQUENCY OF ENCOUNTER OF EACH ORIENTED RECEPTIVE-FIELD CLASS. Several of the other changes we observed in MD rabbits could be attributed to a failure to develop mature inhibitory mechanisms. For example, within the sample of orientation-selective cells recorded in MD rabbits, the percentage of SI cells is relatively high. SI cells are characterized by a spatial organization that is limited to one response class—on or off—and they do not have the antagonistic adjacent areas characteristic of SII cells. SI cells may be formed by converging input of uniform cells in the lateral geniculate nucleus (LGNd) and SII cells by converging input of concentric LGNd cells.

Concentric cells in the LGNd develop later in ontogeny than uniform cells (43), and their development is delayed by MD, but there is no evidence available on the effects of MD on their receptive-field size or on the strength of their antagonistic surrounds (10). If the antagonistic surrounds of concentric LGNd cells are weaker in MD rabbits, then some of the SI cells encountered in MD rabbits might be cells that would have become SII under normal rearing conditions. There is some evidence that deprivation may alter a cell's destiny. For example, in MD cats, LGNd cells are encountered that are physiologically identified as X-cells but have morphologies characteristic of Y-cells. Friedlander et al. (19) suggest that these cells, destined to be Y-cells, develop different physiological characteristics in the deprived environment.

Alternatively, the loss of antagonistic regions may involve a breakdown of inhibition at the cortical level rather than at the level of the LGNd. There is evidence that blocking of \( \gamma \)-aminobutyric acid, an inhibitory interneuron in cat visual cortex, alters receptive-field properties of visual cortical cells (25, 48–51).

RECEPTIVE-FIELD SIZE OF ORIENTATION-SELECTIVE CELLS. Among orientation-selective cells there was a dramatic increase in receptive-field size in SII and complex cells but not in SI cells. Such increased receptive-field sizes are not observed in LGNd of MD rabbits (10). We speculate above that some SI cells might be cells originally destined to become SII cells but with afferent input from LGNd cells with weakened antagonistic surrounds. Nevertheless there must be a significant sample of cells originally destined to become SI cells which show no increase in receptive-field size. In either case, inhibitory mechanisms at the cortical level might be less important in the determination of receptive-field size in SI than in SII and complex cells. The increased receptive-field size in SII and complex cells probably reflects a failure of inhibitory mechanisms. This increased receptive-field size has also been observed in binocularly deprived (BD) cats (53, 60) and has been attributed to a loss of inhibitory sidebands. No increased receptive-field size was reported in dark-reared cats (15, 28) but these studies on deprived cats were done in different laboratories and may have involved different methodologies of receptive-field mapping.

DIRECTION SELECTIVITY OF ORIENTATION-SELECTIVE CELLS. Another major change in orientation-selective cells in MD rabbits was the significant decrease in direction selectivity. In cats, the effects of early deprivation on direction selectivity are not well documented. Most studies of MD in cats do not discuss
direction selectivity (61, 62). In dark-reared cats (28) all receptive types showed a loss of direction selectivity. In BD cats, Watkins et al. (60) noted a significant percentage of cells in the monocular segment that were orientation selective and were also direction selective, but the sample of cells with mappable receptive fields was very low. Overall, in these deprived cats, direction selectivity appears to survive better than orientation selectivity, whereas in rabbits the reverse is true. This difference is discussed further below.

**Nonorientation-selective cells**

Note that this group of cells is not encountered with any frequency in cat or primate visual cortex outside of lamina IV, and it is this group of cells that is least affected by MD in rabbits. I did observe a significant increase in receptive-field size and a significant increase in the frequency of encounter of movement-sensitive cells. Both of these changes could be attributed to decreased efficacy of inhibitory processes. However, there was no change in the organization of internal or surround inhibition in these cells. Overall these cells appear to develop normally in most respects in the absence of pattern vision.

**Comparison of the effects of deprivation on cat and rabbit visual cortex**

It is apparent that, in both cats and rabbits, the effects of deprivation are not uniform; subpopulations of cells are differentially affected by the deprivation. In cats, these subpopulations have been related to parallel X-, Y-, and W-pathways, with the effects of deprivation being most pronounced in Y-cell pathways (31, 47). In the rabbit, although there is some evidence for a similar organization of visual pathways, the criteria used for the cat are not wholly applicable (1). Attempts to classify cortical cells in the rabbit as X-, or Y-pathway cells have been made only recently (20). Thus, although it is clear that, in the rabbit, some cells are more susceptible than others to the effects of deprivation, a direct comparison of subpopulations of cells in cat and rabbit cannot be made.

In the above discussion of receptive-field characteristics in MD rabbits I have referred to some findings in cats raised with MD, BD, dark-rearing, or stripe-rearing. However, since I recorded from the monocular segment of MD rabbits, the only study in cats that is strictly comparable to our study is that of Wilson and Sherman, who recorded from the monocular segment of area 17 in MD cats. The authors note that it was very difficult to record any cells in the monocular segment contralateral to the deprived eye, and their sample is therefore very small. In contrast, I experienced no noticeable difference between normal and MD rabbits in ease of recording. Wilson and Sherman (1977) reported that within the sample of cells they did record there was a high percentage of abnormal cells; among the few normally responsive cells, most had simple fields, and very few had complex fields.

In rabbits, I observed only a slight reduction in frequency of encounter of SII cells, which are equivalent to the type of simple cell most frequently recorded in the cat in terms of laminar organization and spatial characteristics. This was also a small reduction in complex cells, but a large increase in SI cells. SI cells are seen more rarely in cat than in rabbit (35) and are not discussed by Wilson and Sherman (1977). There was no increase in unresponsive or “abnormal” cells.

These data suggest that the effects of MD are much more severe in cat than in rabbit. However, in the cat the effects of BD are quite different from the effects of MD even in the monocular segment. Watkins et al. (60) have hypothesized that the two types of
deprivation involve different developmental mechanisms. They note that the effects of BD are similar in both the binocular and the monocular segments and are much more severe in cat monocular cortex than are the effects of MD. In BD cats less than 12% of cells had normal receptive fields and there was a loss of both orientation selectivity and direction selectivity.

A major question that arises from these findings is whether this observation of more severe effects, and the hypothesis of different developmental mechanisms involved in BD, also applies to the rabbit—an animal in which the visual system is predominantly monocular. Previous studies of MD in the binocular segment in the rabbit suggest that binocularity is not so susceptible to disruption in rabbits than cats, but this study needs to be repeated in view of more recent analyses of cortical binocular interactions in the normal rabbit cortex (24). The critical experiment to approach this question is to compare recordings in monocular cortex obtained in BD rabbits with those obtained in BD cats. A study of monocular cortex in BD rabbits is now underway in our laboratory. Meanwhile, our comparison of the data now available indicate that the effects of MD are much less severe in rabbit than in cat.

Mechanisms of direction selectivity in normal and deprived rabbits

Our study indicates that direction selectivity of orientation cells is reduced in MD animals. In the rabbit, strobe rearing constitutes an even more disruptive environment during development than does MD (39, 40, 41). Although direction selectivity is significantly reduced in MD rabbits, the reduction is much greater in strobe-reared animals. Thus, our data suggest that there may be different populations of cells: Some develop direction selectivity regardless of environmental influences, some develop direction selectivity in MD but not in strobe-reared rabbits, and some only develop normally in a normal environment. Others have also noted the existence of subpopulations of cells which differ in their susceptibility to environmental manipulations (22, 58). We have suggested previously (34, 36) that in the rabbit, direction selectivity is more susceptible to disruption by deprivation than is orientation selectivity. It is noteworthy that, in normally developing rabbits, (34, 36) direction selectivity reaches adult levels later than orientation selectivity, whereas in cat, direction selectivity appears to develop earlier, (although there are conflicting data; see Refs. 8, 23, 42, 46). Our evidence that, in rabbits, orientation selectivity is quite resistant to the effects of deprivation while direction selectivity is vulnerable support the hypothesis that the two are subserved by different mechanisms. In the cat, it has been shown that orientation and direction sensitivity differ in their critical periods (3, 17), their response to strobe rearing (13, 14), and the reversibility of their disruption (Ref. 15; but see Ref. 38). Orientation and direction sensitivity also differ in their response to iontophoretic application of bicuculline, a GABA antagonist, which disrupts direction selectivity but not orientation selectivity (48, 51). These data suggest that in the rabbit, inhibitory mechanisms involved in the organization of direction selectivity are disrupted by MD, but are disrupted even more powerfully by strobe rearing. Other evidence that MD involves some disruption in inhibitory mechanisms is found in the observations, discussed above, of increased receptive-field size and increased frequency of encounter of receptive-field types (SI and movement) in which inhibitory mechanisms may play a less significant role than in other receptive-field types. Intracortical inhibition is believed to be mediated by Y-cells in cats and it is the Y-system that is most affected by deprivation in cats. There is conflicting evidence on the effects of MD on intracortical inhibition in cats (for review see Ref. 47) but the weight of the evidence (57, 62) is that there is a deficiency in inhibitory processes in MD cats. Our data indicate a similar but much less severe, deficiency in inhibitory processes in MD rabbits.

CONCLUSION

Three major questions arise from the present study. One is why, in the rabbit, direction selectivity appears more vulnerable to deprivation than orientation selectivity. A second is why the effects of MD are so much less severe in rabbits than in cats. A third is whether the effects of BD on monocular cortex in rabbits will be more severe than the effects of MD, as they are in cats, or whether rabbits will differ from cats in this respect since the rabbit visual system is predominantly monocular. Some of these issues
are now being studied and should provide further insight into the role of both competitive and inhibitory processes during normal and abnormal development.

ACKNOWLEDGMENTS

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