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Physiological normality of the retina in visually deprived cats

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Cats deprived of visual experience by neonatal suture of the eyelids develop physiological abnormalities in the visual cortex[6,15,16], superior colliculus[13] and lateral geniculate nucleus (LGN)[8]. In seeking to determine the site of the physiological impact of visual deprivation it is of obvious interest to know the effect of deprivation on the physiology of the most peripheral visual centre, the retina. The physiological abnormality found in the LGN of visually deprived cats is the partial functional disappearance from the LGN of one subgroup of relay cells, the so-called Y-cells[8]. In the normal cat Y-cells in the LGN receive their retinal drive from a functional subgroup of retinal ganglion cells[2,7] also called Y-cells[4,7], which are distinguished from other ganglion cells by the high conduction velocity of their axons[2,5,7,12] and by several properties of their receptive fields, particularly their large size[2,4,5] and 'non-linear' spatial organization[3,4].

The present experiments were designed to test whether Y-type ganglion cells are present in the visually deprived retina and, if so, whether any abnormality was apparent in their numbers, in their receptive field properties or in the conduction velocities of their axons. The same tests were also applied to ganglion cells of the other two recognized types, X-cells[4,12] and W-cells[12]. By all tests the retinal ganglion cells of deprived cats appear to be functionally normal, indicating a more central origin for the physiological abnormalities of visually deprived cats.

Experiments were performed on adult cats anaesthetized with ether during surgery and with nitrous oxide (70% N_2O–30% O_2) during recording, and paralyzed during recording by continuous intravenous infusion of gallamine triethiodide and dichloride toxiferine[1]. Seven cats were used. Five were monocularly deprived (MD) of visual experience by suture of the eyelids of one eye[14]. Two were binocularly deprived (BD) by suture of the eyelids of both eyes. The suturing was done on the eighth postnatal day, and the eyelids were left sutured until just before recording, 12–18 months later.

The cats were mounted in a stereotaxic headholder facing a tangent screen 1 m

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from the cat's eye. The activity of retinal ganglion cells was recorded with 4 *M* NaCl-filled micropipettes inserted into the intact eye using an apparatus described previously[11]. For recording field potentials, low impedance (3–6 MΩ) micropipettes were selected. For recording single-unit activity, higher impedance (> 10 MΩ) micropipettes were selected, for reasons described previously[10]. Stimulating electrodes were placed stereotaxically in the optic chiasm (OX) and optic tract (OT)[11,12], to activate the retinal ganglion cells antidromically. Receptive fields of single ganglion cells were plotted on the 1 m tangent screen, and classified as Y-, X- or W-type, using techniques and criteria described previously[2,7,12].

Methylene blue-stained whole-mount preparations were made of the retinas of two MD and two BD cats[9].

Antidromic field potentials. The antidromic field potentials elicited in the retina by electrical stimulation at OX and OT provide evidence that Y-type retinal ganglion cells are present in visually deprived retinas in normal numbers and with axons of normal conduction velocity. First, the *shapes* of the field potentials provide evidence that Y-cells are present in normal numbers. Fig. 1A shows the field potential recorded

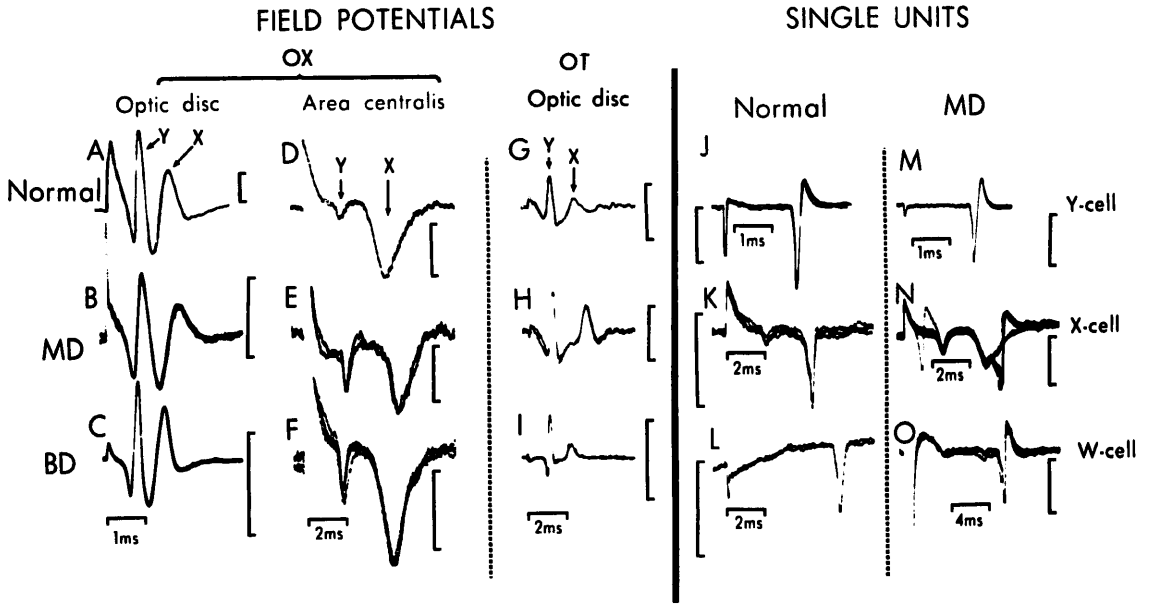


Fig. 1. Antidromic field potentials and unit responses recorded in the retina of normal, MD and BD cats following stimulation at the optic chiasm (OX) or tract (OT). A–C: field potentials recorded at the optic disc following stimulation of the optic chiasm, in normal (A), MD (B) and BD (C) cats. The components of the potentials generated by the axons of Y-cells and of X-cells are indicated by arrows; D–F: antidromic field potentials recorded at the area centralis following OX stimulation in normal (D), MD (E) and BD (F) cats; G–I: field potentials recorded at the optic chiasm following OT stimulation in normal (G), MD (H) and BD (I) cats; J–L: antidromic responses of a Y-cell (J), X-cell (K) and W-cell (L) recorded in the retina of a normal cat, following OX stimulation; M–O: antidromic responses of a Y-cell (M), X-cell (N) and W-cell (O) recorded in the retina of an MD cat following OX stimulation. For all traces recording polarity is negative upwards and the vertical scale represents 0.5 mV, except for Fig. 1E, where the vertical scale represents 0.2 mV. The recordings from MD cats were all from the deprived eye.

at the optic disc in a normal retina, following OX stimulation. Previous work (summarised in refs. 11, 12) has shown that this potential comprises two di- or triphasic components (indicated by arrows in Fig. 1A), the earlier component being generated by the fast-conducting axons of Y-cells, the second by the slower-conducting axons of X-cells. Fig. 1B and C shows the analogous field potentials recorded in the deprived eye of an MD cat and in a BD cat. Both Y- and X-cell components of the potentials appear normal in shape and relative amplitude. There is no evidence of a decrease in the relative amplitude of the Y-cell component of the potential which might be expected if the number of Y-cell axons in the optic nerve were reduced by deprivation. Similarly, the antidromic field potential recorded at the area centralis of a normal retina following OX (Fig. 1D) or OT stimulation differs characteristically in waveform and relative amplitude from those recorded in peripheral retina. The area centralis potential also has two components generated by faster- and slower-conducting axons, but each component is monophasic positive in shape, rather than di- or triphasic, and the later, X-cell, component is relatively more prominent than in potentials recorded at the optic disc or in peripheral retina[11]. The area centralis potentials recorded in the deprived eye of an MD cat and in a BD cat following OX stimulation are shown in Figs. 1E, F. Again there appears to be no evidence of abnormality in the shape or relative amplitudes of these potentials. Figs. 1G–I show the field potentials recorded following OT stimulation at the optic disc in a normal cat (Fig. 1G), in the deprived eye of an MD cat (Fig. 1H) and in a BD cat (Fig. 1I). Each potential comprises early (Y-cell) and late (X-cell) components, and the Y-cell component is as prominent in the deprived cats as in the normal. Thus the axons of Y-cells seem to be present in normal numbers in the optic tract of MD and BD cats. The traces in Fig. 1G–I were recorded following stimulation of the contralateral OT. The field potentials generated in MD and BD cats by stimulation of the ipsilateral OT were also apparently normal.

Second, the *latencies* of the antidromic field potentials give some indication of the conduction velocities of Y- and X-cell axons in visually deprived cats. The latencies of the early (Y-cell) components of the potentials in Fig. 1A–C vary little (range 0.7 msec–0.9 msec) suggesting that the conduction velocities of Y-cell axons in the optic nerve of deprived cats are close to normal. Similarly the latencies of the Y-cell components of the OT-elicited potentials in Figs. 1G–I vary little (0.85 msec–1.1 msec), suggesting that the conduction velocities of Y-axons in the optic tract of deprived cats are also close to normal. The intraretinal conduction velocities of Y- and X-cell axons were estimated (as previously[11]) by noting the increase in the latencies of the early and late components of the antidromic field potential as the position of the recording electrode was moved progressively away from the optic disc. The intraretinal velocity of Y-axons was estimated in this way to be 3.7 m/sec in an MD cat and 4.2 m/sec in a BD cat; both values are within the normal range. For X-cell axons, intraretinal velocity was estimated at 1.9 m/sec in both MD and BD cats. Again this value is close to the normal range[11]. The latencies of the early and late components of the field potential recorded at the area centralis also vary little (range 1.9–2.1 msec for the early component, 4.3–4.8 msec for the late component) between

the normal cat (Fig. 1D) and deprived cats (Figs. 1E, F). These latencies included both extra- and intraretinal conduction times, so that in deprived cats both the extra- and intraretinal velocities of area centralis cells appear to be close to normal.

The latencies of the late (X-cell) components of the field potentials in Figs. 1A–I vary considerably more than the early component latencies, *e.g.* 1.3–1.65 msec in Figs. 1A–C, 1.85–2.5 msec in Figs. 1G–I. Nevertheless, the range of X-cell axon conduction velocities among normal and deprived animals suggested for example by the OT latencies (assuming[11] a conduction distance of 37 mm between the OT stimulating site and the optic disc), is 15 m/sec–21 m/sec, comparable with the normal range reported by previous workers[11].

Single unit recording. Single units with antidromic latencies typical of Y-cells were encountered in the retina of deprived cats with normal frequency. That is, when micropipettes with impedances of 3–6 MΩ were used Y-cells comprised 75% of the 48 units whose activity was isolated; of the remainder 11 were X-cells and one was a W-cell (*cf.* ref. 10). Both Y- and X-cells appeared functionally normal, and indistinguishable in latencies (Figs. IJ, K, M, N) and receptive field properties from Y- and X-cells observed in normal retina. Thus, Y-cells had larger receptive field centres than X-cells, and responded 'phasically'[5] or 'transiently'[2] to a stationary centred stimulus. The response of X-cells to the same stimulus was, conversely, 'tonic'[5] or 'sustained'[2]. Y-cells showed the same responsiveness to fast-moving stimuli described previously[2,7] while X-cells were, as previously described, consistently less responsive to fast-moving stimuli.

With higher impedance micropipettes (> 10 MΩ) Y-, X- and W-type ganglion cells were all observed in both MD and BD cats. The relative frequencies of the three types among 31 cells recorded in and near the area centralis in MD cats were 4 Y-cells (13%), 21 X-cells (67%) and 6 W-cells (20%). These percentages are close to those

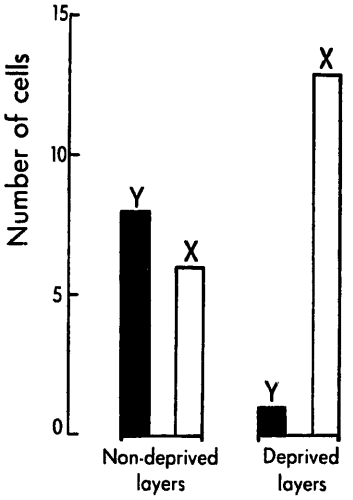
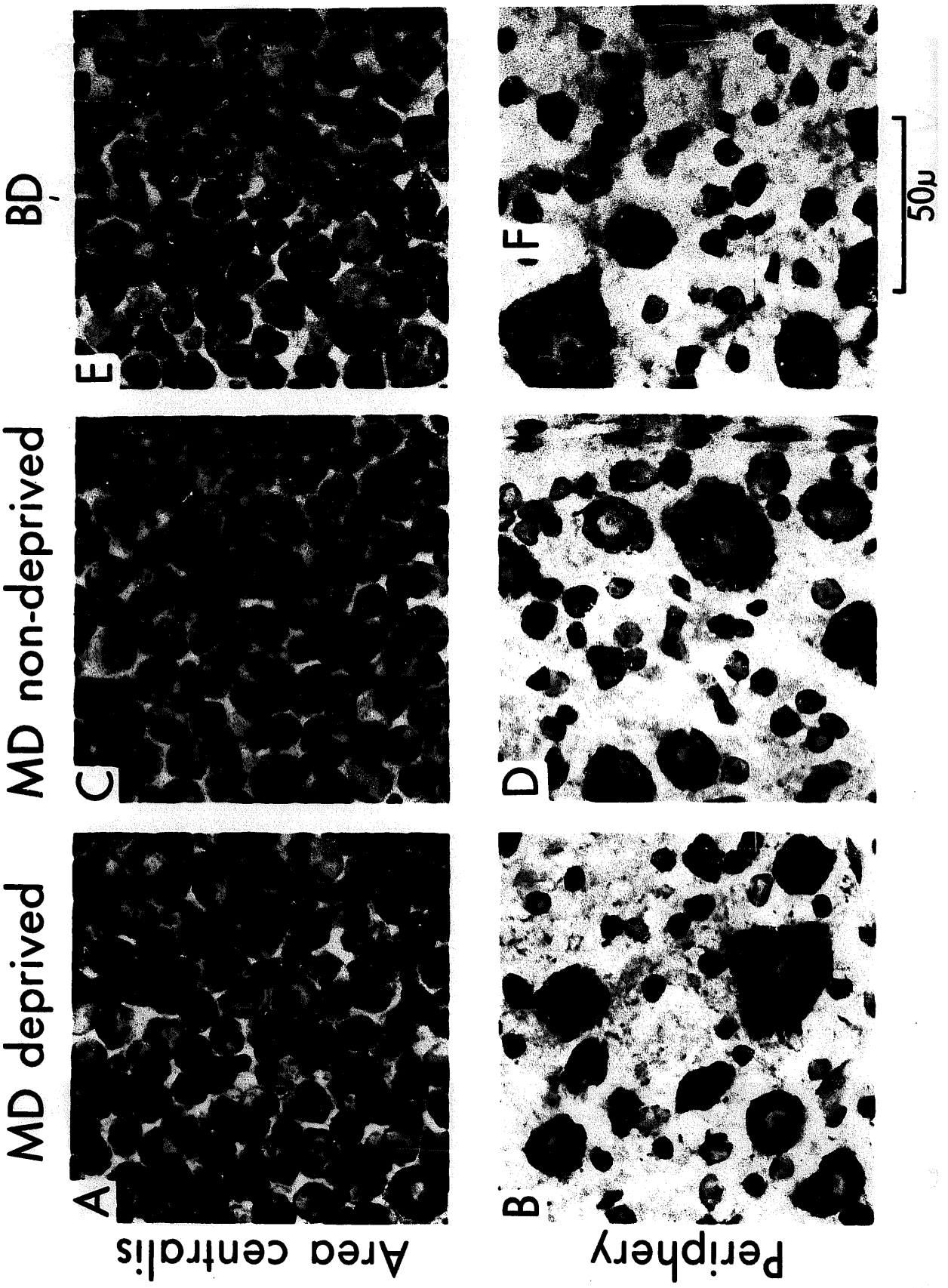


Fig. 2. Frequency histograms showing the numbers of Y- and X-cells recorded in the lateral geniculate nucleus contralateral to the deprived eye of an MD cat. Samples of cells driven by the non-deprived and deprived eyes are shown separately. The number of Y-cells encountered in the layers receiving input from the deprived eye is markedly reduced, as reported previously[8].


MD deprived
MD non-deprived
BD
A
C
E
B
D
F
Area centralis
Periphery
50μ

reported for normal retina[10]; the percentage of Y-cells is in fact somewhat higher than in the normal, perhaps because of the small sample. Only units whose spike waveforms showed an initial positive inflection were included for this analysis; *i.e.* recording from axons were excluded. The W-cells observed in deprived cats had antidromic latencies (Fig. 1L, O) and receptive field properties similar to those described in the normal[12]. That is, the antidromic latencies of W-cells to OX stimulation were always longer than Y- and X-cell latencies, indicating that their axons are slower-conducting than the axons of Y- and X-cells, and their receptive fields included both ON–OFF and centre–surround types, as described previously[12].

LGN control. In one of the 5 MD cats recordings were made in the LGN contralateral to the deprived eye, after antidromic field potentials and 15 single units had been recorded in the retina of the deprived eye. We sought to show that the functional loss of Y-cells from the LGN, reported earlier[8], was present in the same cat in which the deprived retina had been investigated and appeared to be normal. Five tracks were made through the LGN and the activity of 28 LGN cells was isolated so that the receptive field of each cell could be plotted and classified as Y- or X-type. Of the 28 cells, 14 were driven by the non-deprived eye, and comprised 8 Y-cells and 6 X-cells. Of the 14 driven by the deprived eye, 13 were X-cells and only one was a Y-cell (Fig. 2). These distributions differ significantly ($P < 0.02$ on a χ^2 test). The functional loss of Y-cells from the LGN thus seems as severe in this cat as previously reported[8].

Histological appearance of the ganglion cell layer. Seen in whole mount preparations (Fig. 3) the size and density of ganglion cells in the retinas of BD and MD cats appeared quite normal, both at the area centralis and in peripheral retina. Specifically, cell size and density did not appear to differ between the deprived and non-deprived retinas of an MD cat (*cf.* Fig. 3A–D) or between the MD retinas and a BD retina (Fig. 3E, F) or between any of the deprived cat retinas and a normal retina (*cf.* Figs. 7 and 8 in ref. 9).

The present results indicate that the development of the retina is unaffected by the deprivation of visual experience effected by lid suture. The ganglion cells of the deprived retina appear normal in cell body size, in receptive field properties, in axonal conduction velocities and in the relative frequency of Y-, X- and W-cells. The impact of visual deprivation on the development of the afferent visual pathway seems therefore to be exerted at a site or at sites central to the retina and optic tract.

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Fig. 3. Areas of methylene blue-stained retinal whole mounts from the deprived (A, B) and non-deprived (C, D) eyes of an MD cat, and from the eye of a BD cat (E, F). For each retina areas are shown of the ganglion cell layer at the area centralis (A, C, E) and at a location 3 mm temporal to the area centralis (B, D, F).

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