Increased Receptive Field Size in the Surround of Chronic Lesions in the Adult Cat Visual Cortex

Visual cortical lesions destroy the target cells for geniculocortical fibers from a certain retinotopic region. This leads to a cortical scotoma. We have investigated the receptive fields of cells in the visual cortex before, 2 days and 2 months after focal ibotenic acid lesions in the adult cat visual cortex and have found signs of receptive field plasticity in the surroundings of the chronic but not the acute and subacute excitoxicotic lesions. In the subacute state (first two days post lesion) receptive field sizes of cells at the border of the lesion were reduced in size or remained unchanged. Remapping of cortical receptive fields 2 months later revealed a number of cells with multifold enlarged receptive fields at the border of the lesion. The cells with enlarged receptive fields displayed orientation and direction selectivity like normal cells. The size increase appeared not specifically directed towards the scotoma; however, the enlarged receptive fields reduce the extent of a cortical scotoma, since previously unresponsive regions of the visual field activate cortical cells at the border of the lesion. This late receptive field plasticity could serve as a mechanism for the filling-in of cortical scotomata observed in patients with visual cortex lesions.

Materials and Methods

Preparation and Surgical Procedures

Adult cats (n = 8, 2.5–5 kg) were anesthetized with ketamine hydrochloride (20 mg/kg) and xylazine hydrochloride (2 mg/kg) for initial surgery (tracheotomy and insertion of a catheter into the femoral artery for acute recording experiments or tracheal intubation and flexible access to the brachial vein for placing a chronic lesion). Anesthesia was further maintained by respiration with a 70/30 mixture of N2O/O2 with halothane (0.2–0.6%) throughout the 1–4 day experiments. Nutrition and paralysis was provided by continuous vascular infusion of a Ringer solution containing alcuronium chloride (Alloferin®, 0.06 mg/kg/h) and glucose (1.25%). Pressure points and wound margins were locally anesthetized by infiltration of a long-lasting anesthetic (xylocaine), and the animals were fixed in a stereotaxic apparatus. A trepanation of 2 × 10 mm was centered at P2/L3 above the visual cortex. The physiological state of the animals and adequacy of anesthesia were ensured by continuous monitoring of arterial blood pressure, pulse rate, flow and mixture of O2/N2O and halothane used for respiration, end tidal carbon dioxide and body temperature. All experiments were carried out in accordance with the guidelines published in the European Communities Council Directive (86/609/EEC, 1986).

Ibotenic Acid Lesions

Ibotenic acid (1%, 300–500 nl) was pressure injected through a glass micropipette with 18 µm tip diameter to introduce small focal cortical lesions. Two types of lesion experiments were performed. In the subacute experiments (n = 5) recordings were made before lesioning and 2–3 days post lesion from identical cortical positions (n = 15) with a linear array of seven electrodes. These animals were kept under continuous anesthesia in darkness except for the testing of visual receptive fields. In the chronic experiments, control recordings were made prior to lesioning (n = 14). After injection of ibotenic acid the trepanation was closed with the original bone piece and the wound was closed by suturing all anatomical layers. Wound margins were again infiltrated with the long-lasting local anesthetic. When infusion of relaxant was discontinued spontaneous respiration was re-established, respiration with O2/N2O/halothane was stopped and the animals were extubated. The cats were then kept undeprieved in large rooms in the animal house in a visually rich environment; they did not suffer from any visible disabilities. The chronic effects of the lesions on RFs (n = 18) were investigated between 55 and 76 days post lesion, when the animals were taken back into the experiment using the same procedures described above.
proteins (MAPs) as neuronal marker, and glial fibrillary acidic protein immunohistochemistry with antibodies against microtubuli-associated Masson’s trichrome stain for electrode track reconstruction or treated and cut in serial sections (5 µ). Consecutive sections were stained with glass micro-Ω filled with 3 M NaCl in the chronic experiments, and in the subacute experiments with a linear array of individually movable platinum-in-glass electrodes (‘Eckhorn-Array’, Thomas Recording, Marburg, Germany) with 1 mm interelectrode distance that were left in the same places before and after lesioning. Responses were processed by a spike discriminator (Alpha-omega, Israel) and fed into a personal computer for storage and further processing.

Retinal landmarks (optic disc with main vessels, area centralis) were backprojected to a tangent screen with an ophthalmoscope. Back-projections were repeatedly monitored to monitor eventual small drifts in eye position throughout the experiments.

Mapping of topography and size of the monocular receptive fields (Fig. 2) was carefully performed by hand with a stationary or flickering small light bar (0.3–0.5° × 3–5°). To functionally characterize the receptive fields, visual stimuli were monocularly presented on an oscilloscope 28 cm in front of the eyes. Light bars of optimal width (0.3–0.8°) and length (1.5–10°) were generated with a Picasso CRT image generator (Innsifree, Cambridge, UK) and moved under computer control in two directions at eight orientations (2.25° intervals) in pseudorandom order; peristimulus time histograms (PSTHs) were computed from 5 or 10 trials for each orientation and polar diagrams were constructed from the peak response rates obtained for each of the 16 directions of motion.

Histology
At the end of the experiments the animals were killed by an overdose of anesthetic and perfused with 4% paraformaldehyde in phosphate buffer (pH 7.4). The cortical region containing the lesions and electrode tracks was blocked, kept overnight in 0.025 M PBS at 4°C, embedded in paraffin and cut in serial sections (5 µ). Consecutive sections were stained with Masson’s trichrome stain for electrode track reconstruction or treated for immunohistochemistry with antibodies against microtubuli-associated proteins (MAPs) as neuronal marker, and glial fibrillary acidic protein (GFAP) to reveal glia cells. For immunohistochemistry (slide-method) the paraffin-embedded sections were dewaxed in xylene and transferred through a descending ethanol series into PBS. After treatment with n-Gt (normal goat, Dako) and n-Hrs (normal horse, Sigma) antiserum for 1 h, the sections were reacted with the primary antibodies (1:200) overnight (MAP-2, clone HM-2, Sigma; GFAP, clone GA5, Boehringer-Mannheim), and linked to biotinylated goat-anti-rabbit and horse-anti-mouse (Vectostain-Camon) antibody (1:200, 1.5 h). Detection was performed with a standard ABC kit (Vectostain-Camon) 1:100 in PBS for 1.5 h. The DAB reaction was used to visualize immunohistochemical labeling (0.5 mg DAB + 10 µl 0.5% H2O2). Sections were cleared in xylene and coverslipped with Depex (Serva).

The size of the lesions was measured from the serial sections and the electrode tracks were reconstructed to show their position relative to the border of the lesions.

Results
Lesions
The injection of ibotenic acid resulted in focal lesions characterized by a loss of all neurons as shown 76 days post lesion with MAP immunohistochemistry and with neurofilaments as neuronal markers (MAP2, NF200, Fig. 1A,B). The antibodies against MAP2 and NF200 indicate the loss of neuronal processes within the lesioned area, and at the same time show the unchanged density of neuronal elements at the immediate border of the lesion. The GFAP staining shows a glial scar that has developed in response to the excitotoxic lesion in the region free of neurons (Fig. 1C). The neuronal loss was already evident within the first 2 days post lesion not only by the complete functional loss around the injection site but also by the disintegration of neurons histologically visible in Nissl-stained sections. The average diameter of the lesions (determined from the Nissl stains) in the five acute and three chronic animals was 2.9 mm (range 2.1–4.3 mm). The average depth of the lesions was 1.6 mm (range 1.25–2.0 mm); they typically extended to the layer 4/5 border.

Figure 1. Immunohistochemical verification of a chronic lesion 76 days after ibotenic acid injection into cat striate cortex (coronal sections). (A) Immunostaining with a monoclonal antibody against MAP2 clearly delineates the loss of neurons (cortical layers indicated on the left). (B) The region free of labeling by a polyclonal antibody against neurofilaments (NF200) closely resembles the area devoid of MAP2. (C) The increased density of glial cells in the region corresponding to neuronal loss indicates the glial scar. Scale bar corresponds to 0.5 mm.
Normal Receptive Field Topography and Acute Lesion Effects

Before lesioning, RFs were mapped with penetrations spaced by ~1 mm both in subacute and chronic experiments, and the topography and size of RFs were carefully determined. The RF position of cells in the visual cortex (area 17) migrated from the upper to the lower visual field when penetrations were displaced in the AP plane from posterior to anterior (Fig. 2).

Figure 3 shows typical RF maps before and after an acute ibotenic acid lesion. We recorded with a linear array of seven electrodes spaced by 1 mm that was left in place throughout the 2–3 day experiment. RF position and size were mapped for each electrode and the ibotenic acid lesion was applied close to one of the recording electrodes (no. 6). At this and the neighboring electrodes neuronal activity ceased after a period of strongly increased firing. After the cats had been kept in darkness for 2 days the RFs were remapped at the still active electrode positions and no substantial changes in RF size or location were observed; this was true for the example shown in Figure 3 as well as for the other subacute experiments (Fig. 8). In two cases where the lesion was placed in the middle of our electrode array (not shown) gaps of retinal representations (1° and 3°) were found in the RF map.

Chronic Changes of Receptive Field Size

Figure 4 summarizes a chronic experiment with 55 day survival time between lesioning and final experiment. The localization of penetrations was documented by photography of the cortical surface on the day of ibotenic acid injection (Fig. 4A). This enabled us to retest the same cortical positions after 55 days survival time (Fig. 4B). In Figure 4A,B the recording sites are indicated, together with the lesion site on the cortical surface. Figure 4C shows the RF locations and sizes as mapped before lesioning. The cells were vigorously responding and the location and outmost borders of the excitatory RF could be exactly mapped. The largest RF found in each penetration is outlined and labeled with the number of the respective electrode penetration. The ibotenic acid injection was applied at the location of recording site 1 (Fig. 4A,C). In the experiment, after 55 days survival time this location is again labelled as recording site 1 (Fig. 4B,D). In this location no activity was encountered up to a recording depth of 1500 μm where the first visually driven background activity was recorded. This was considered as the lower border of the lesion and the penetration was discontinued. During all the other penetrations anterior or posterior to the lesion site single cells with crisp responses, direction specificity and sharp tuning for orientation were recorded in the supragranular cortical layers. The location and spatial extent of the RFs of these cells could be determined with the same accuracy as the RFs during the initial lesioning experiment in the same animal. At the recording sites 2 and 2a, up to 1 mm anterior of the border of the lesion, individual cells displayed impressingly increased RF sizes (Fig. 4D), although in the same penetrations we also encountered single cells with rather normal RF size (the smallest and largest fields obtained in the individual penetrations are shown). RFs returned to normal pre-lesion sizes at the most anterior recording site (no. 3). Due to the normal decrease in RF size towards the area centralis, there should be a continuous decrease in average RF size from the most anterior to the most posterior penetration.

The findings of the experiment with 55 days survival time (Fig. 4) were completely reproduced by the results obtained in the experiment with 76 days survival time shown in Figure 5. Here the lesion was placed between the pre-lesion penetrations 2 and 3 (Fig. 5A,B). The pre-lesion RFs showed a regular enlargement from posterior (penetration 1a close to the area centralis) to 4 mm anterior (penetration 4). Seventy-six days post lesion (Fig. 5C) penetrations 2 and 3 were situated adjacent to the lesion (as revealed from histology). These penetrations and the penetration 0.5 mm anterior (penetration 4) revealed enlarged receptive fields very similar in size to the preceding experiment (Fig. 4D). There was no gap in the retinal representation. In addition, we performed a series of penetrations 0.8 mm further lateral (Fig. 5D) where we did not obtain enlarged RFs except for penetration 7 that was situated directly lateral to the ibotenic acid lesion.

We computed PSTHs and polar plots to quantitatively verify the RF width as well as orientation and direction specificity. Figure 6 shows examples of two RFs of cells matched for
recording depth and eccentricity before and 76 days after lesioning. The control RF (Fig. 6A; from penetration 2 in Fig. 5A, B) yielded a width of ∼3° and was characterized by a strong direction specificity and orientation selectivity; the RF lateral to the chronic lesion (Fig. 6B, from penetration 7 in Fig. 5D) displayed strong orientational and directional tuning and an unusually large RF width of ∼8°. Both simple and complex cells were among the cells with enlarged RFs.

**Cortical Location of Cells with Increased RF Size**

The cells with increased receptive field size were situated close to the border of the chronic lesions as evident from the relative position of the recording sites to the ibotenic acid injection site. This close vicinity is shown histologically for penetration 7 of Figure 5 by the reconstructed electrode track passing down at the very border of the lesion as visualized in a Nissl-stained section (Fig. 7). From the known recording depth and the limits of the lesion seen in the Nissl stain we can conclude that the cell with the enlarged RF (Fig. 5D) was located directly at the border of the cortical lesion.

In all experiments the receptive fields stayed approximately normal in size in the subacute situation (tested in cats that were kept in darkness for 2 days) but many were found increased in size after ∼2 months survival time in a visually varied environment. Figure 8 shows the RF width after lesioning as a percentage of the width determined before lesioning at matched recording sites, i.e. 100% indicates no change, values >100% indicate enlargement, values <100% shrinkage of RFs after lesioning. The percentage values were chosen to normalize for the changes in RF width with eccentricity in the visual field. With the seven-electrode array left in place from before to 2 days after the lesion the mean size of 15 RFs stayed unchanged anterior and posterior to the lesion (mean 101.1%, range 75–156%). The scatter of absolute RF sizes remained unchanged as well (all values in degrees before/after: mean 3.6/3.5, median 3.2/3.2, range 2–6.4/2–5.6, SD 1.32/1.06). This indicated, on average, no change in size within the first 2 days following the lesion. When comparing the RF sizes before lesioning (n = 8) with the sizes found at the same topography in the visual field 55 and 76 days after lesioning (n = 18), the overall range of sizes changed to 64–385% with a mean of 182%. The larger scatter and increased mean of RF sizes proved to be due to the RFs of cells within a distance of ∼1 mm from the border of the lesion. While the RF width remained constant (size close to 100% with respect to size before lesioning) 1 mm anterior as well as 1 and 2 mm posterior, there was a mean increase to 188% at the posterior...
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border, and to 182 and 282% respectively at the anterior border and 0.5 mm away (Fig. 8). While close to the lesion 13/14 RFs were larger than the mean of all pre-lesion RFs by up to 7.8°, the RFs recorded 1–2 mm away were exactly in the range of the average pre-lesion RF sizes (~0.8° to +0.2°). We could not detect

Figure 5. (A) Schematic drawing of the cortical surface with penetrations as shown in (B)–(D). As for the experiment shown in Figure 4, penetration sites were photographically recorded and are shown on a sketch of the cortical surface. Recording sites before ibotenic acid injection (X) and 76 days later (filled circles) across the lesion (broken circle) are numbered 1–4, while a more lateral series of post-lesion penetrations is numbered 5–8. (B) RF map in the left visual field (VM, vertical meridian; HM, horizontal meridian) before application of ibotenic acid between pre-lesion penetrations 2 and 3. The map of the excitatory receptive fields was primarily obtained with hand-held stimuli and confirmed by subsequent computer-assisted stimulation and peristimulus time histogram averaging (see Fig. 6 for an example). Increasing numbers indicate penetrations from posterior (p) to anterior (a) in area 17 (above) and corresponding RFs in the visual field (below). Increasing numbers indicate penetrations from posterior (p) to anterior (a) in area 17 (above) and corresponding RFs in the visual field (below). (C) Recording across the same region 76 days post lesion. Penetrations were placed with respect to the same landmarks as in (A) and the positions relative to the lesion site were later histologically verified (see penetration 7 shown in Fig. 7A,B). Note the strongly enlarged RFs in the surrounding of the ibotenic acid lesion (penetrations 2–4). (D) A series of penetrations 0.8 mm lateral to those in (B). Again the RF close to the border of the lesion in penetration 7 is significantly enlarged (see also Fig. 6).

Figure 6. Peristimulus time histograms (PSTHs) and polar plots of a pre-lesion control cell and a cell at the border of the chronic (76 day) lesion with matched eccentricity in the visual field. (A) Control cell recorded in penetration 2 of Figure 5B. The cell was recorded at a depth of 400 µm. The light bar (10 × 0.4°) was stationary during the first 400 ms, moved with a 5° amplitude for 800 ms (6.3°/s) through the RF in one direction and back in another 800 ms. The RF width as read from the peak in the PSTH was ~3°. The second histogram shows the responses for the orthogonal orientation. The cell shows significant orientation and direction selectivity. (B) This cell was recorded at the border of the chronic lesion (Fig. 5D, penetration 7) in a depth of 500 µm. The peak response rate is similar to the control cell at matched eccentricity. The light bar (6 × 0.4°) was stationary for 1 s and moved for 2 s with an amplitude of 20° across the receptive field (10°/s) and back during the following 2 s. The optimal and orthogonal orientations are shown. The polar plot reveals a clear orientation specificity and a very strong direction selectivity. The RF width as measured from the response to the moving light bar was ~8°, and significantly wider than RFs of control cells and cells further away from the lesion (Fig. 5).
any correlation between the size of the lesions and the amount of RF reorganization at the border of the lesion.

Discussion

Lesions of the Striate Cortex

Many studies have made use of striate cortex lesions in the adult for various reasons; however, this is the first study to investigate receptive field size at the border of chronic lesions in the striate cortex. Earlier studies have employed surgical striate cortex lesions in adult cats and monkeys to investigate area 17/18 interactions (Donaldson and Nash, 1973), cortical blindness (Keating, 1977), visual capacity (‘blind sight’) remaining after the lesion (Weiskrantz and Cowey, 1970; Weiskrantz, 1978), intracortical axonal degeneration (Creutzfeldt et al., 1977), retinal degeneration (Dineen and Hendrickson, 1981), hypertrophy of dorsal lateral geniculate nucleus (dLGN) and alterations of retinal input after striate cortex lesions (Hendrickson and Dineen, 1982; Dineen et al., 1982), projection patterns of surviving neurons in the dLGN (Cowey and Stoerig, 1989), and deactivation of area MT (Kaas and Krubitzer, 1992), as well as small excitotoxic striate cortex lesions to study the effects on eye movements (Newsome et al., 1985). In an earlier study we have used small acute heat lesions in the striate cortex to disclose the effects of lateral signal processing on cat single visual cortex cells (Eysel et al., 1987). In the present study we have applied excitotoxic striate cortical lesions to study possible changes in receptive field size that could lead to a functional reduction of the size of a cortical scotoma. While receptive fields of cells at the border of the lesion remained unchanged during the first 2 days, a significant enlargement of receptive fields was observed when the same cortical region surrounding the lesion was investigated after 2 months.

Feedforward and Feedback Pathways for Reorganization

When cell death takes place in the striate cortex, the visual field region represented by the lesioned part of cortex is lost, but the un severed geniculocortical afferents still offer the complete retinal topography as feedforward input and also as feedback input via area 18 to the surviving cortical cells at the border of the lesion (Fig. 9A). It is therefore possible that surviving cortical cells at the border of the lesion in area 17 can ‘learn’ to respond to inputs from retinal regions that have been deprived of their original cortical targets. This could make the lost information from the intact retina available again in the primary visual cortex for further cortical processing.

There are two main possible pathways of reorganization as indicated in Figure 9B. The chronic and acute inactivation functionally eliminates local target cells and the lateral intracortical network, but does not affect the afferent geniculocortical system, which spreads collaterals over several millimeters giving rise to clusters of contacts (Gilbert and Wiesel, 1979; Freund et al., 1985), and area 18, which receives direct geniculocortical inputs in the cat (Holländer and Vanegas, 1977; Geisert, 1980).
and provides ‘feedback’ connections that cover a much larger area of retinal projection in striate cortex than is represented by their region of origin in area 18 (Salin and Bullier, 1995). Therefore cells at the border of a lesion presumably receive subthreshold inputs outside their original receptive field from collaterals of geniculocortical afferents and the recurrent area 18 to 17 pathway. Under normal conditions, however, the inputs from both widespread excitatory systems that would lead to a widening of receptive fields in area 17 remain functionally below threshold. The finding of enlarged receptive fields at the border of cortical lesions raises the question why these cells do develop exceptionally large excitatory RFs, whereas under control conditions RF areas in that cortical region were significantly smaller.

**Increased Excitability at the Border of the Lesion**

Increased excitation seems to be one key step to initiate reorganization at the border of cortical lesions. In the first week post lesion we have observed increased spontaneous and visual excitability in the immediate surrounding of cortical lesions (Eysel and Schmidt-Kastner, 1991), and in the somatosensory cortex of the rat we have seen increased N-methyl-D-aspartate-mediated EPSPs at the border of such lesions in vitro (Mittmann et al., 1994). This increased excitability at the border of lesions could facilitate changes of synaptic efficiency that can lead to the enlargement of receptive fields by activation of previously subthreshold (‘silent’) synapses. However, passive facilitation alone does not seem sufficient to lead to the increase of RF sizes since the observed expansion of receptive fields did not occur spontaneously within the first 2 days when the animals were kept under continuous anesthesia and darkness. This indicates that use and/or time are necessary to bring about the RF size increases. In vivo we have observed long-term potentiation (LTP)-like increases of RF size after repetitive visual stimulation in the normal cortex of the anesthetized adult cat (Eysel et al., 1998a,b). Increased excitability and reduced inhibition in the surround of lesions could facilitate such mechanisms to become effective during coactivation of the target cell from its RF proper and from adjacent RFs via geniculocortical input or area 18 feedback collaterals, leading to increased efficacy of the synapses and consequently to the observed expansion of RFs. Indeed, signs of increased LTP have recently been described with in vitro field potential recordings at the border of somatosensory cortex lesions after a survival time of 14 days (Hagemann et al., 1998).

Cortical inhibition has been proposed in general to control plasticity in the adult mammalian visual cortex (Jones, 1995). Accordingly, reduction of lateral inhibition at the border of a lesion could additionally support plasticity. This hypothesis is also related to the suggestion of Artola and Singer (1987) that inhibitory synapses at layer III neurons could reduce synaptic plasticity by shunting excitatory postsynaptic currents. In fact, Hirsch and Gilbert (1993) often observed failure to induce LTP-like changes in the cat visual cortex in vitro when the responses included strong inhibition. In another in vitro study, Kirkwood and Bear (1994) ascribed a critical role to inhibitory intracortical circuits for gating of visual cortical plasticity at the network level. Inhibition might even lead to depression of the respective inputs due to the described voltage dependence of long-term plasticity (Artola et al., 1990) in the rat visual cortex in vitro. In fact, strongly decreased GABAergic IPSPs have been described close to the border of cortical lesions (Mittmann et al., 1994), and GABA receptors are downregulated in the surrounding of cortical lesions (Schiene et al., 1996).

**Temporal and Spatial Aspects of Reorganization**

A transient increase in visual receptive field size was reported for cells at the border of excitotoxic lesions in area MT of the monkey between 6 and 13 days post lesion (Wurtz et al., 1990). In our study the changes in RF size were more persistent; however, we do not know when the increase of RF size began with normal use of vision during the 2 months survival time. As shown in Figure 4D the enlarged fields were found not only directly adjacent to but also ~1 mm distant from the border of a lesion. By demonstrating the degeneration of axons after localized striate cortical lesions, Creutzfeldt et al. (1977) have elegantly shown the range of the direct anatomical effects of a small lesion in area 17 extending horizontally up to 1800 µm in layer III. In addition, the direct lateral extent of inhibitory connections in the upper cortical layers was found in the range of 1–2.5 mm with the large majority confined to 1 mm (Albus et al., 1991; Kisvárday et al., 1997). This lateral range of supposed disinhibitory effects due to loss of inhibition from the lesioned area is in keeping with the distance of 1 mm from the border of a visual cortical lesion at which the peak of increased excitability was observed in vivo 1–7 days after lesioning (Eysel and Schmidt-Kastner, 1991).

**Parallel Effects Following Retinal and Somatosensory Cortex Lesions**

The predominant effect of retinal lesions at striate cortex cells is a significant shift of receptive field topography that leads to a filling-in of the scotoma from the border of the retinal lesion due to lateral signal processing in the visual cortex (Kaas et al., 1990; Heinen and Skavenski, 1991; Kisvärday et al., 1997). This lateral range of supposed disinhibitory effects due to loss of inhibition from the lesioned area is in keeping with the distance of 1 mm from the border of a visual cortical lesion at which the peak of increased excitability was observed in vivo 1–7 days after lesioning (Eysel and Schmidt-Kastner, 1991).

**Figure 9**. Possible mechanisms of reorganization. (A) Simple wiring diagram showing the lesion and possible pathways for reorganization (LGN, lateral geniculate nucleus; A17, area 17; A18, area 18). An acute cortical scotoma (outer circle) is surrounded by small receptive fields (small inner rectangles). During chronic reorganization the RFs enlarge and thus fill-in part of the scotoma (light gray shading), resulting in a scotoma of reduced size (inner circle with dark gray shading).
Terminal sprouting of horizontal axons was observed in the cat visual cortex 6 and more months following retinal lesions (Darian-Smith and Gilbert, 1994). Sprouting of cortical axons has also been observed following radiation lesions of the upper layers in young and adult rabbit striate cortex, where the 3.0–4.5 mm diameter regions completely devoid of nerve cells were invaded by supposedly newly grown nerve fibers within 7 weeks post lesion (Rose et al., 1960). In the present experiments we did not observe nerve fibers inside the lesion with neurofilament immunohistochemistry (Fig. 1B); however, there might be sprouting phenomena involved in the reorganization at the border of the lesion. Regarding the differences between the two types of lesion, it appears important to mention that after the excitotoxic lesion destruction of cells was visible in Nissl stains within the first 2 days, while it took 1–2 weeks until the first histological changes were seen after radiation lesions; moreover, glial cells produced a scar after the excitotoxic lesions, while glia was rare in regions lesioned by radiation.

The somatosensory cortex responds to remote and local lesions in a way very similar to the visual cortex: changes of cortical topography were observed in response to deafferentation (for review, see Kaas, 1991), and Jenkins and Merzenich (1987) reported a complete filling-in of the lost representation of the palm representation by strongly enlarged RFs of cells surrounding a lesion in the primary somatosensory cortex after 129 days in the owl monkey. Such signs of adult plasticity appear to be a general feature of sensory cortices (for review, see Kaas, 1991; Eysel, 1992).

**Reducing the Size of the Scotoma**

Patients with visual field loss due to vascular or traumatic postgeniculate damage with homonymous defects that were quantitatively determined with static and dynamic visual field perimetry were trained in the border regions of their residual visual fields by repeated stimulation to improve light-difference thresholds (Zihl and von Cramon, 1979) or by locating targets within the blind field region (Zihl and von Cramon, 1985). Both types of training led to a reduction of the scotoma size and consequently an enlargement of the visual field in the majority of patients. The recovery was specifically dependent on practice; this was also the case in a study where patients with homonymous visual field deficits were exposed to a computer-based restitution training that specifically activated the border region of the visual field defect (Kasten and Sabel, 1995; Kasten et al., 1998). It was hypothesized that this recovery might take place at the level of the striate cortex.

The enlarged RFs of cells at the border of the cortical lesion represent a mechanism for functional recovery of primarily lost parts of the visual field and thus lead to a reduction of the size of a scotoma as shown in Figure 9B. This is a non-redundant, functionally useful reorganization since inputs that have lost their target cells are reconnected to surviving cortical cells. The absolute increase of RF size (Figs 4, 5) observed here would allow for a shift of the border of a scotoma by ~3–4°, which is in the range of the 4.9 ± 1.7° recently observed in patients treated with computer-based visual field training (Kasten et al., 1998). This suggests that the long-term plasticity of cells at the border of visual cortical lesions may represent a model in the mature visual system of the cat for the long-term reduction of visual field defects observed in human patients.

**References**


Notes

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