Effects of Feedback Projections From Area 18 Layers 2/3 to Area 17 Layers 2/3 in the Cat Visual Cortex

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[1]Laboratorios de Neurociencia y Computacion Neuronal (asociados al Instituto Cajal-CSIC), Facultad de Medicina y Servicio Neurofisiologia Clinica-Complejo Hospitalario Universidad de Santiago de Compostela, Santiago de Compostela E-15705, Spain; [2]Departamento de Ciencias de la Salud II, Universidad de A Coruña, A Coruña E-15006 Spain; and [3]Department of Optometry and Vision Sciences, University of Manchester Institute of Science and Technology, Manchester M60 1QD, United Kingdom

Martinez-Conde, Susana, Javier Cudeiro, Kenneth L. Grieve, Rosa Rodriguez, Casto Rivadulla, and Carlos Acuña. Effects of feedback projections from area 18 layers 2/3 to area 17 layers 2/3 in the cat visual cortex. *J. Neurophysiol.* 82: 2667–2675, 1999. In the absence of a direct geniculate input, area 17 cells in the cat are nevertheless able to respond to visual stimuli because of feedback connections from area 18. Anatomic studies have shown that, in the cat visual cortex, layer 5 of area 18 projects to layer 5 of area 17, and layers 2/3 of area 18 project to layers 2/3 of area 17. What is the specific role of these connections? Previous studies have examined the effect of area 18 layer 5 blockade on cells in area 17 layer 5. Here we examine whether the feedback connections from layers 2/3 of area 18 influence the orientation tuning and velocity tuning of cells in layers 2/3 of area 17. Experiments were carried out in anesthetized and paralyzed cats. We blocked reversibly a small region (300 μm radius) in layers 2/3 of area 18 by iontophoretic application of GABA and recorded simultaneously from cells in layers 2/3 of area 17 while stimulating with oriented sweeping bars. Area 17 cells showed either enhanced or suppressed visual responses to sweeping bars of various orientations and velocities during area 18 blockade. For most area 17 cells, orientation bandwidths remained unaltered, and we never observed visual responses during blockade that were absent completely in the preblockade condition. This suggests that area 18 layers 2/3 modulate visual responses in area 17 layers 2/3 without fundamentally altering their specificity.

INTRODUCTION

To date, very little is known about the role of feedback connections in the visual system, either at the corticocortical or corticothalamic levels. In the cat visual cortex, area 17 and adjacent area 18 are reciprocally connected (Bullier et al. 1984; Ferrer et al. 1988, 1992; Salin et al. 1992, 1995; Squatrito et al. 1981; Symonds and Rosenquist 1984a,b). Input from area 18 can drive visual responses from area 17 cells in the absence of a direct geniculate input (Mignard and Malpeli 1991). This connection (often called a "feedback" connection) arises from two levels: one from layer 5 of area 18 and projecting to layer 5 of area 17, and the other from layers 2/3 of area 18 projecting to layers 2/3 of area 17 (Henry et al. 1991; Salin and Bullier 1995). Focal lidocaine blockade in layer 5 of area 18 can affect

both the orientation and velocity selectivity of cells within layer 5 of area 17 (Alonso et al. 1993a,b). Here we investigate the effect of focal GABA blockade of layers 2/3 of area 18 on the visual responses of cells in layers 2/3 of area 17 to sweeping bars of various orientations and velocities. Preliminary data have been presented in abstract form (Acuña et al. 1995).

METHODS

Animal preparation

Experiments were carried out on 32 adult cats (1.8–3.0 kg). The animals were anesthetized with halothane (5% for induction; 1.5–2% for surgery and 0.1–0.5% for maintenance) in NO_2 (70%) and O_2 (30%) and paralyzed with gallamine triethiodide (40 mg iv for induction, 10 mg $\cdot$ kg^{-1} $\cdot$ h^{-1} iv for maintenance). Lidocaine hydrochloride with adrenaline was administered subcutaneously to all wound margins, and the ear bars of the stereotaxic frame were covered with lidocaine gel (1%). Solutions of atropine methonitrate and phenylephrine hydrochloride were applied to each eye to dilate the pupils, paralyze accommodation, and retract the nictitating membranes. Zero power contact lenses, 3-mm artificial pupils, and supplementary lenses were used to bring the eyes to focus on a tangent screen at a distance of 57 cm. End-tidal CO_2 levels (maintained between 3.8 and 4.2%), electroencephalogram (EEG), electrocardiogram (ECG), and temperature of the animal (maintained between 37.5 and 38.5°C) were monitored continuously throughout the experiment. All of the experimental procedures were approved by the National Committee (Spain) from the International Council for Laboratory Animal Science, protocol 86/809/EEC.

Simultaneous recording and iontophoretic administration of drugs

Single-unit extracellular activity was recorded through a tungsten microelectrode placed in layers 2/3 of area 17 of visual cortex. In area 18, single-unit activity from layers 2/3 was recorded simultaneously through the central barrel of a seven-barreled micropipette, with a tip broken back to 3–10 μm diam. The recording barrel contained 3 M NaCl. Five of the six other barrels contained γ-aminobutyric acid (GABA, 0.5 M, pH 3.5), and the sixth barrel was filled with Pontamine sky blue (PSB, 2% wt/vol in 0.5 M sodium acetate solution) for histological reconstruction of the micropipette position. Focal reversible blockade was achieved by the iontophoretic application of GABA through one or more barrels of the micropipette (range: 30–100 nA). The extent of the blockade was <300 μm in radius, as shown by control experiments in which a second recording micro-

electrode was placed at various distances from the micropipette. To avoid leakage from the micropipette, we applied a small retention current of 5–25 nA in the polarity opposite to the ions being injected. In the recovery phase, visual responses were tested again in both cells, 5–8 min after cessation of GABA iontophoresis.

Although single-cell recording in area 18 was necessary to differentiate between cells in layers 2/3 and layer 4 (or deeper), GABA blockade certainly inhibited cells with receptive fields beyond the receptive field of the cell we were recording from. Thus orientation selectivity, direction preference, receptive field position, and velocity tuning of individual cells in area 18 may not be exactly the same for the local population of inactivated cells.

Visual stimulation system

Cells of both areas were first studied qualitatively by hand-mapping. Each cell was classified as simple or complex (Hubel and Wiesel 1962), and ocular dominance was measured on a five-point scale (Wilson and Sherman 1976), simplified from the original seven-point scale of Hubel and Wiesel (1962). Each pair of cells was quantitatively studied using computer-controlled stimuli (Visual Stimulation System, Cambridge Electronic Design, Cambridge, UK). Stimulus contrast $[(L_{max} - L_{min})/(L_{max} + L_{min})]$ was held to within a nonsaturating range (0.36–0.7), with a mean luminance of 14 cd/m^2. The receptive fields of all cells were within 12° of the area centralis.

Experimental protocol

Because of time limitations, each pair of cells was tested either for velocity or orientation, but not both. We studied three successive conditions for each pair of cells: control (preblockade), GABA (in which we infused GABA into area 18), and recovery. During the velocity experiments, visual stimuli consisted of bars of light with optimal width and orientation for each cell, sweeping at six different velocities (2, 4, 8, 15, 25, and 32°/s). Bar length (10°) always extended beyond the receptive fields in the two areas. When the preferred orientation for the cell in area 17 differed from the preferred orientation for the cell in area 18, we ran the control and recovery conditions twice (once for each orientation). During the blockade situation, the cell in area 18 was inactive, so we optimized the stimulus orientation for the cell in area 17 only (we ran the test only once, even if cells in areas 17 and 18 had different orientations). Each velocity was presented 15 times, in a randomly interleaved fashion.

During the orientation experiments, visual stimuli consisted of 10° long bars of light with optimal width and velocity for each cell, sweeping at six different orientations at intervals of 30° (each orientation having 2 directions of movement). When the preferred velocity for the cell in area 17 differed from the preferred velocity for the cell in area 18, we ran the control and recovery conditions twice (once for each velocity). In the blockade situation, the stimulus velocity was optimized for the cell in area 17 only. Each orientation was presented 10 times in a randomly interleaved fashion.

Statistical analysis

Visual responses were measured in spikes per second for each velocity or orientation tested. We collected peristimulus time histograms (PSTHs) with binwidths of 100 ms. In the velocity experiments we compared the peak bin in each histogram for every condition and across the various velocities. It was necessary to compare only peak rates of firing when comparing responses in the velocity domain, because trials with slow velocities are longer in duration and therefore collect larger numbers of spikes than trials with fast velocities, even if the instantaneous firing rate was higher for the fast velocities. In the orientation experiments the trials were of constant duration, so we compared both the peak firing rate (as in the velocity tests), as well as the average firing rate for the entire sweep of the bar. Both methods

generated precisely the same results. We considered there to have been a change in the response of each area 17 cell, during area 18 blockade, when the change in response was statistically significant ($P \leq 0.05$ using both 2-way ANOVA Friedman test and Wilcoxon rank sum test). If changes were less than significant ($P > 0.05$), we categorized these cells as "unchanged." All cells used in the analysis were moreover required to recover completely from the blockade, so that the control and recovery conditions were not significantly different ($P > 0.05$) in both area 18 and 17. This was necessary to be sure that any changes in firing rate in area 17 were due to the administration of GABA in area 18, rather than to changes in EEG activity during our experiment, or other factors. Orientation tuning curves were smoothed and normalized to calculate their half bandwidths at half height (Orban 1984).

Histological reconstruction

Recording sites were marked (area 17 microelectrode: 30 μA 20 s; area 18 multipipette: PSB application, 5 mA 30 min). At the end of the experiment animals were overdosed with pentobarbital and their brains removed and fixed by immersion in 10% formaldehyde in normal saline. After cryoprotection in 30% sucrose solution, 60-μm frozen sections were Nissl stained. Areas and laminae marked were then identified (Garey 1971).

RESULTS

Velocity experiments

We tested 31 pairs of cells for bars sweeping at various velocities. During area 18 blockade, 17/31 (55%) area 17 cells showed increased responses, 5/31 (16%) cells showed decreased responses, and 9/31 (29%) cells showed no response changes.

An example of an increased response is illustrated in Fig. 1A. This area 17 complex cell had an optimum response to bars sweeping at a rate of 4°/s. The other cell of the pair (Fig. 1B), an area 18 complex cell, had an optimum response to an appropriately oriented light bar drifting at ~15°/s. The two cells had the same orientation and direction preferences and had the same ocular dominance. The area 17 cell receptive field was partially overlapped (24%) by the receptive field of the cell in area 18. During area 18 blockade the responses of the area 17 cell increased for all velocities to which the cell responded without blockade, and no responses were seen to the highest velocities tested in any condition. Figure 2 shows the PSTHs from which Fig. 1 was derived. The lack of activity of the area 17 cell to stimuli of velocities of 25 and 32°/s is striking (Fig. 2, A–C), given the relatively robust responses seen in the cell in area 18 (Fig. 2, D and E).

An example of a decreased response in an area 17 complex cell is illustrated in Fig. 3A. The cell in area 18 (Fig. 3B) was simple, and its receptive field almost completely overlapped (87%) that of the area 17 complex cell. The two cells had the same orientation preference (although with opposite direction preference), and ocular dominance differed by one point. During GABA blockade of area 18 the response of this area 17 cell was reduced, except for the response to the lowest velocity tested, which was unaffected by the blockade. Figure 4 shows the PSTHs corresponding to these two cells.

In 9/31 cell pairs, no effect of blockade in area 18 was seen in area 17. An example of this is illustrated in Fig. 5. The receptive fields of these two cells were completely nonoverlapping, which may explain the lack of changes in responsive-
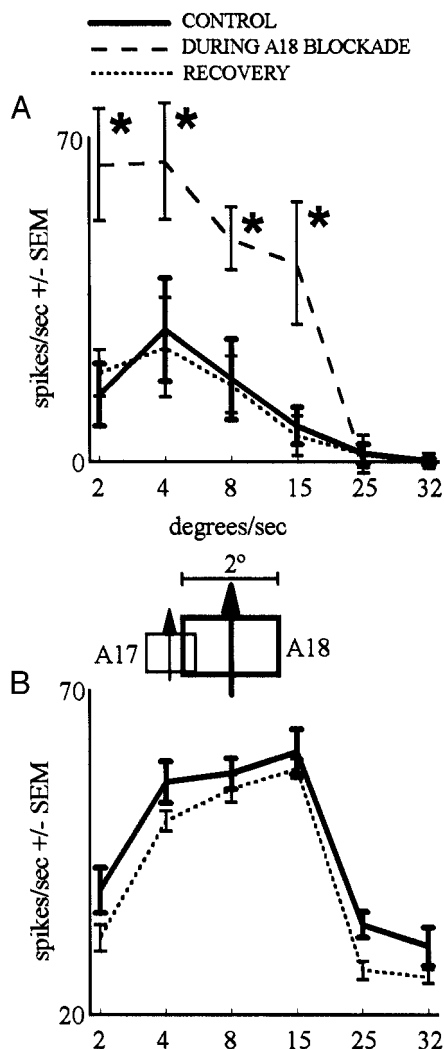
FIG. 1. Response increment in the velocity domain. *A*: continuous thick line, velocity tuning curve for an area 17 cell tested for the velocities shown. Responses of this cell peaked at 4°/s. Dashed line, responses during GABA blockade of area 18. There was a significant increase (asterisk: $P \leq 0.05$) to all of the velocities to which the cell responded during the control (2, 4, 8, and 15°/s). Dotted line, recovery after the end of GABA application. *B*: continuous thick line, responses from an area 18 cell simultaneously recorded and to the same stimulus. Dotted line, recovery of the responses of the area 18 cell after GABA application. *Inset*: dimensions, retinotopic location, and preferred orientation and direction of the receptive fields of both cells.

ness in the area 17 cell. The optimum velocity response for this area 17 complex cell was 15°/s (Fig. 5*A*). The area 18 cell (Fig. 5*B*) was a simple cell, with an optimal response at 32°/s or perhaps higher. Both cells had the same orientation selectivity but opposite direction preference and differed in ocular dominance by one point.

Orientation experiments

We recorded from 66 cell pairs to test area 18 blockade effects on area 17 in the orientation domain. Most area 17 cells [49/66 (74%)] showed clear changes in their responses during area 18 blockade. Decreased responses were found in 27 (41%) cells, increased responses in 22 (33%) cells, and 17 (26%) cells showed no changes.

Figure 6 is an example of an area 17 cell with an increased

response to area 18 blockade: before the blockade (*A*), during the blockade (*B*), and after the blockade (*C*). The optimum orientation was between 270 and 300°. Responses were increased especially at the optimum orientations. Figure 6*D* shows the responses of a complex cell recorded simultaneously in area 18 before (solid line) and after the blockade (dotted line). The cell had an optimum orientation of 120°. Most (87%) of the area 17 cell's receptive field was overlapped by the receptive field of the cell in area 18.

Figure 7 illustrates an example of a narrowly tuned area 17
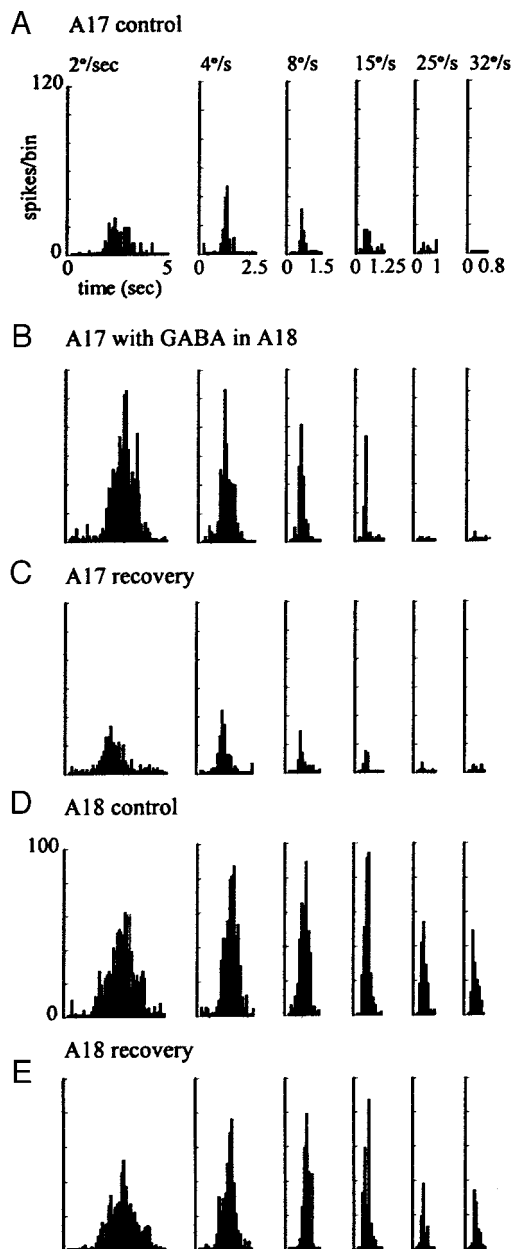

FIG. 2. PSTHs for the cells in Fig. 1. *A*: peristimulus time histograms (PSTHs) for the velocities tested for the area 17 cell from Fig. 1, before area 18 GABA induced blockade. *B*: PSTHs from the responses of the area 17 cell during area 18 blockade. *C*: PSTHs of the recovery of the area 17 cell after the blockade. *D*: PSTHs showing the control responses of the area 18 cell shown in Fig. 1. *E*: PSTHs showing the recovery of area 18 cell after the application of GABA. For each cell the preferred direction of stimulus movement is shown.

cell with a decreased response to area 18 blockade. The optimum orientations of both cells were very similar (although preferred directions of motion were opposite) and their receptive fields almost fully overlapped (89%). During GABA application in area 18 (Fig. 7B), the area 17 cell showed a decrease in response of 50% at the preferred orientation (90°). After the recovery from the blockade, the responses of both cells returned to their preblockade levels.

Some area 17 cells (17/66) showed no changes in their rate of discharge during GABA application in area 18 at any of the orientations tested. Figure 8 illustrates an example on an area 17 complex cell. Unlike the cells illustrated in Figs. 6 and 7 that changed in responsiveness, the receptive fields from these two cells were overlapping only marginally (16%), suggesting that projections from area 18 to area 17 tend to match retinotopically.

Those area 17 cells unaffected by area 18 blockade (Figs. 8 and 5) furthermore illustrate the good stability (statistical stationarity) of responses throughout the different conditions.
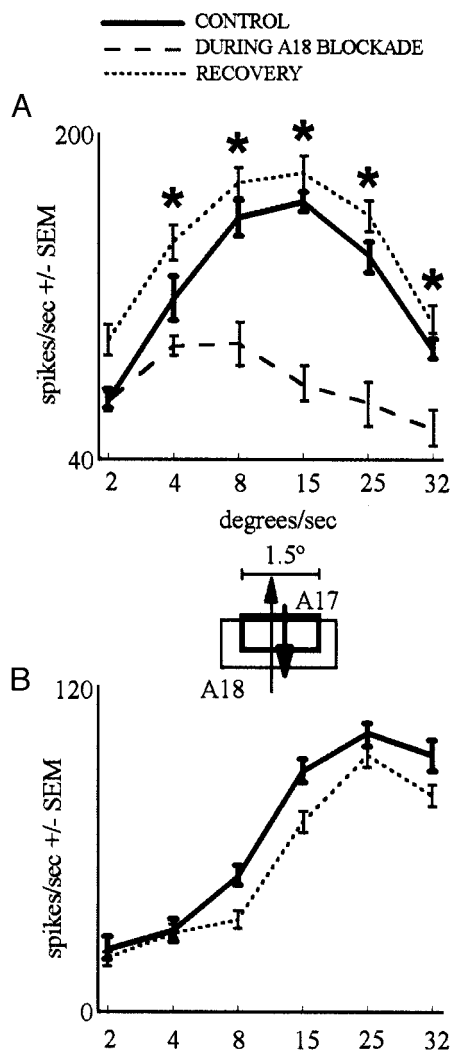

FIG. 3. Response decrement in the velocity domain. A: area 17 cell with decreased responses during area 18 blockade. Responses of this cell peak at ~15°/s in the control condition. During GABA-induced blockade of area 18, there is a significant decrease to stimuli of the velocities 4, 8, 15, 25, and 32°/s. B: responses of the simultaneously recorded area 18 cell before and after GABA application. *Inset*: receptive fields.
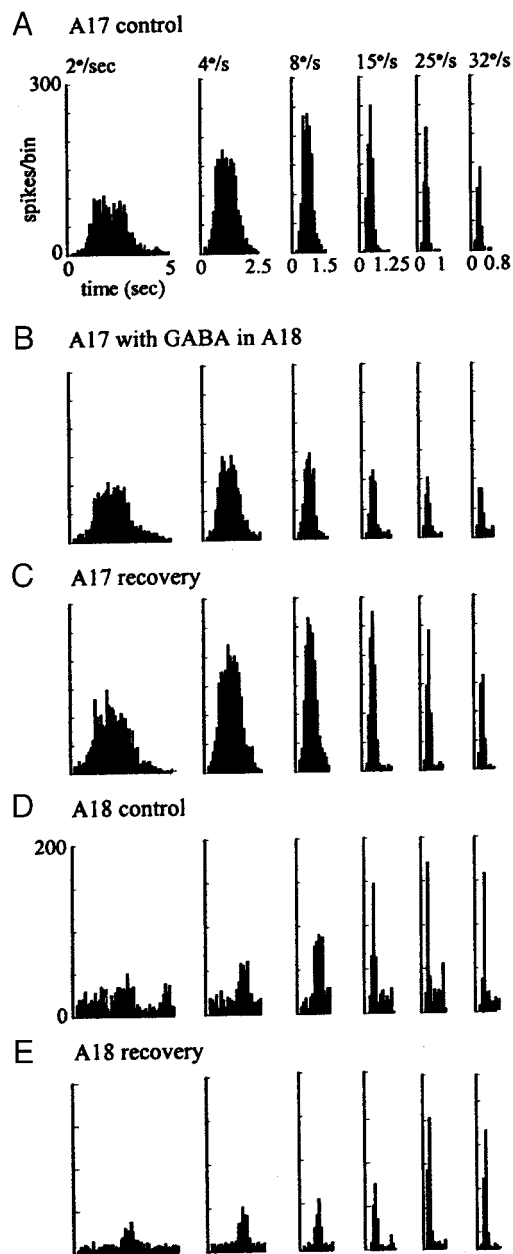

FIG. 4. PSTHs from the responses of the pair of cells illustrated in Fig. 3.

Strength of the effects

We have separated cells with significant changes in response into two groups: one for response increments and one for response decrements. The reason for separating the data in this way is that cells can decrease their rate of discharge up to 100%, but increases in firing rate are not limited to 100%, so comparing the magnitude of these effects in terms of percent change would be inappropriate between groups.

The average peak increase in area 17 responses during area 18 blockade was 127 ± 18% (mean ± SE) in the velocity experiments and 113 ± 23% in the orientation experiments. The average peak decrease in area 17 responses was 63 ± 9% in the velocity experiments and 43 ± 3% in the orientation experiments.

The average P-value (2-way ANOVA Friedman test) for the significant changes was 0.0233 ± 3.887E-03 in the orientation
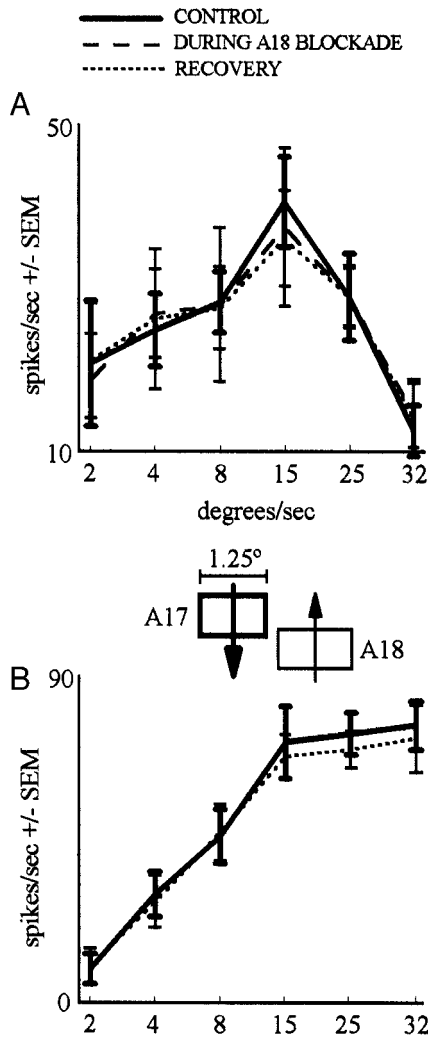
FIG. 5. Absence of changes in the velocity domain. *A*: area 17 cell without significant changes in its responses to any of the velocities tested during area 18 blockade. Responses of this cell peak at 15°/s. *B*: simultaneously recorded area 18 cell before and after the GABA blockade. *Inset*: receptive fields.

experiments and $0.0238 \pm 2.366E{-}03$ in the velocity experiments.

Figure 9 plots the magnitude of these effects for each individual cell in area 17 against their significance.

Width of tuning curves

Velocity tuning curves bandwidths could not be properly measured for most of the cells recorded, because we only tested a small range of velocities to which cells were sensitive. We observed, however, that either most of the velocities to which cells in area 17 responded to (before area 18 blockade) were affected, or none were. Cells did not become sensitive to velocities to which they were insensitive before the blockade. Furthermore, none of the area 17 cells responded during area 18 blockade with an increase in sensitivity to some velocities and a decrease to other velocities.

Similarly, in the orientation domain, we observed no changes in the optimum orientation, and we rarely saw changes in sharpness of tuning. Figure 10 compares the orientation half-bandwidths for the area 17 cells tested with different

orientations ($n = 66$). Optimum orientations of most cells were unaffected by area 18 blockade, and only 8 of 66 cells showed a change in half-bandwidth of $\geq 10°$ during area 18 blockade. Broader tuning curves were found in six of these cells, and sharper tuning curves were found in two cells. One cell showed an increase in half-bandwidth of 41°, but this was a rare exception. As with velocity tuning, none of the cells increased their responses to some orientations and decreased their responses to others.

Retinotopic location between recording sites in areas 18 and 17

As illustrated in Figs. 1, 3, 6, and 7, area 17 cells that changed their responsiveness appeared to be retinotopically related to the cells recorded simultaneously in area 18 (although one should keep in mind that the recordings in area 18 were from single units within a population of blockaded cells). Figure 11*A* shows the amount of overlap between the receptive fields of cells simultaneously recorded in areas 17 and 18. Not surprisingly, the percentage of overlap was larger in the groups that showed increases ($40.69 \pm 6.13\%$; $n = 39$ cells) and
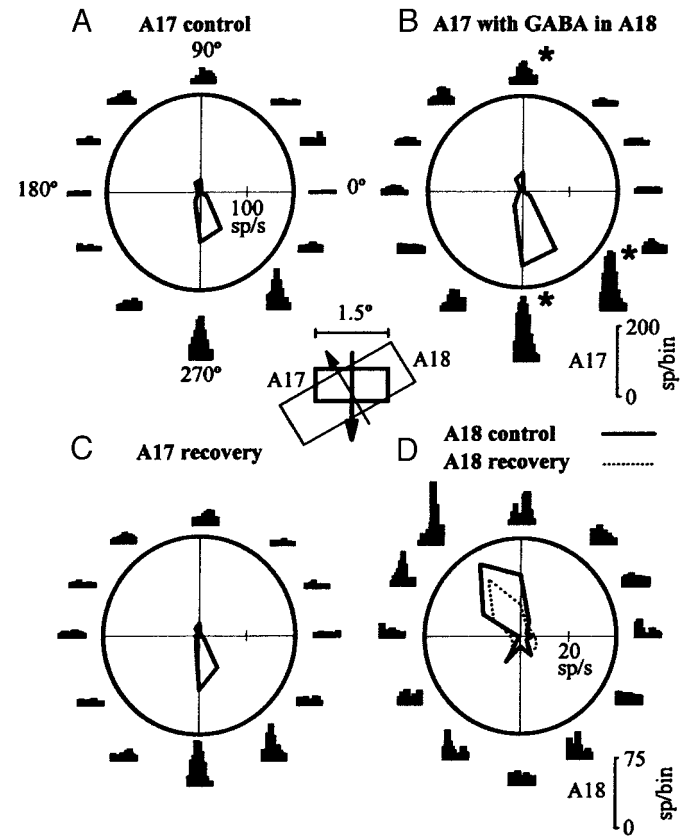

FIG. 6. Response increment in the orientation domain. *A*: orientation tuning curve of a cell from layers 2/3 of area 17. *B*: orientation tuning curve of the same cell during GABA application in area 18. Responses of the cell increased mostly at 270° (52%) and 300° (60%). *C*: orientation tuning curve of the same cell after area 18 blockade. *D*: solid line, control tuning curve of an area 18 cell recorded simultaneously. Dotted line, tuning curve of the same cell after blockade. *Inset*: receptive fields of both cells. In this and subsequent figures, polar plots and PSTHs are shown in each case for all the orientations and directions tested. For clarity, only the preblockade PSTHs are shown in *D*. The number of spikes for PSTHs of areas 17 and 18 are indicated at *bottom* of *B* and *D*, respectively. Bin size: 100 ms. Time base: 1 s.
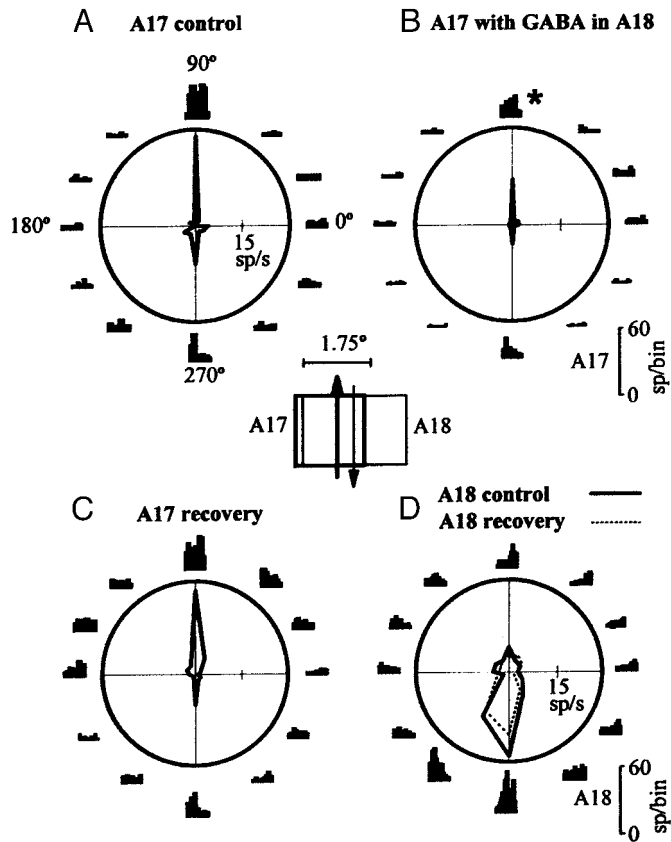
FIG. 7. Response decrement in the orientation domain. *A*: tuning curve of an area 17 cell in preblockade condition. *B*: tuning curve of the same cell during area 18 blockade. There is a 50% decrement in the response of the cell at 90°. *C*: tuning curve of the same cell after area 18 blockade. *D*: solid line, preblockade tuning curve of an area 18 cell. Dotted line, postblockade tuning curve of the area 18 cell. Time base: 3 s. Other conventions as in Fig. 6.
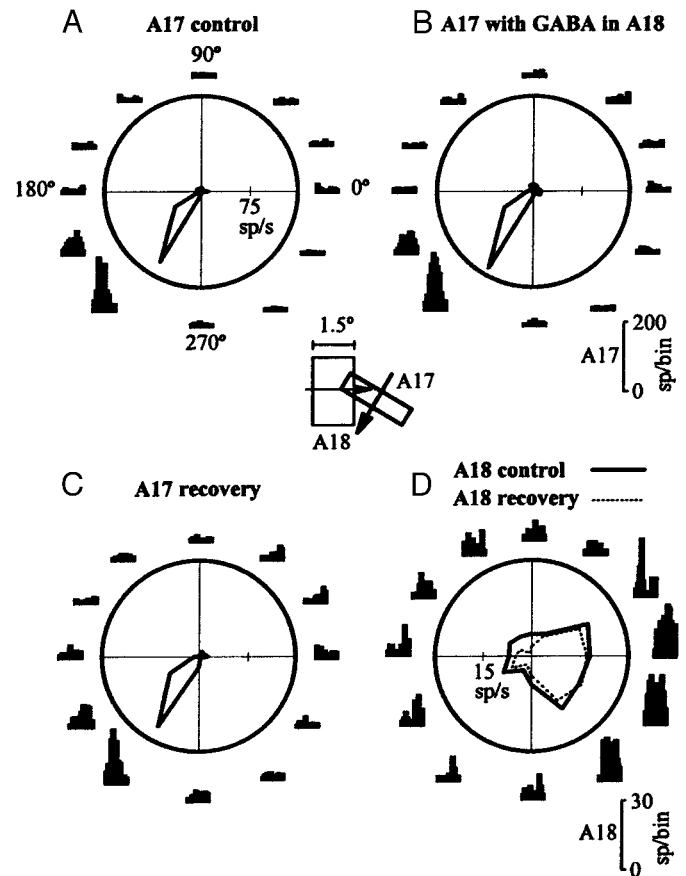

FIG. 8. Absence of changes in the orientation domain. *A*: control tuning curve of an area 17 cell. *B*: no changes are observed in the tuning curve of this area 17 cell during area 18 blockade. *C*: tuning curve of the same cell after area 18 blockade. *D*: solid line, control tuning curve of an area 18 cell recorded simultaneously. Dotted line, tuning curve of the area 18 cell after blockade. Time base: 1.25 s. Other conventions as in Fig. 6.

decreases ($50.71 \pm 6.76\%$; $n = 32$ cells) than in the group of cells that showed no change ($26.38 \pm 7.03\%$; $n = 26$ cells). This difference was statistically significant for the decrease versus the nonchange group of cells ($P = 0.01$; *t*-test). We also calculated the distance (in degrees of visual angle) between the receptive field centers of cells in both areas (Fig. 11*B*). When there was no effect of area 18 blockade, receptive field center distances were relatively larger (mean, 1.63 ± 0.19 SE) than when there was either a decrease in firing (mean, 1.11 ± 0.13 SE; $P = 0.0283$) or an increase in firing (mean, 1.14 ± 0.13 SE; $P = 0.0380$) in area 17. These results are only an approximate indicator, because in each case the receptive fields of the population of cells inactivated in area 18 must have scattered to cover a wider area than that covered by the single receptive field we mapped.

DISCUSSION

General comments

Our results indicate that GABA-induced focal blockade of layers 2/3 of area 18 can produce changes in the responses of cells in layers 2/3 of area 17 to oriented bars, revealing functional connections between the upper layers of both areas, in agreement with previous studies (Mignard and Malpeli 1991). The contribution of these connections to visual perception nevertheless remains unclear. The finding that area 18 block-

ade produced two types of effects on the response of area 17 cells, increases and decreases, may seem puzzling. It suggests a more complex role of area 18 feedback connections than would have been suggested had we found only increases or
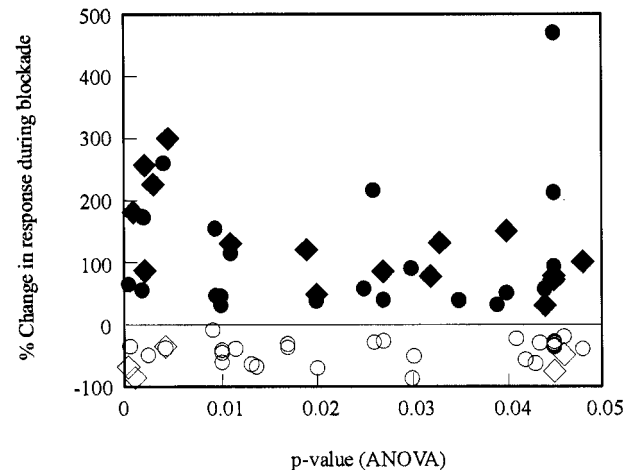

FIG. 9. Peak percentage of change in area 17 responses plotted against the statistical significance of each effect. Positive percentages (● and ◆) correspond to cells that increased their responses. Negative percentages (○ and ◇) represent cells that decreased their responses. ● and ○, cells tested with varied stimulus orientations; ◆ and ◇ cells tested with varied stimulus velocities.
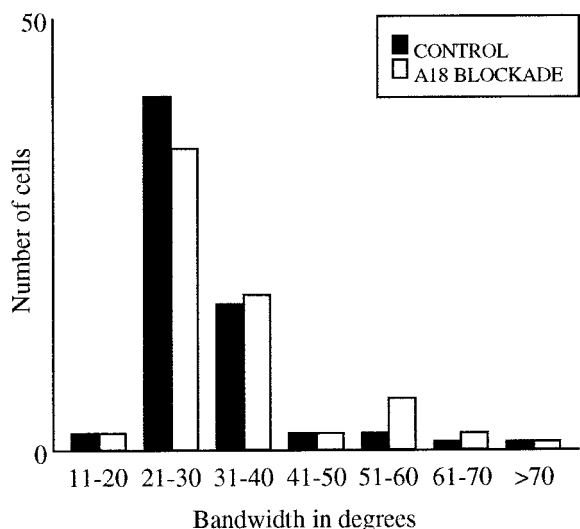
FIG. 10. Orientation selectivity in area 17. Histograms show the distribution of orientation half-bandwidths for area 17 cells ($n = 66$) before (black bars) and during (white bars) area 18 blockade.

decreases in responsiveness in area 17 cells or if we had found changes in only one of the domains, orientation or velocity. As it stands, the only perceptual role we might suspect for the connections between the upper layers from area 18 to area 17 is the modulation of sensitivity in area 17 cells, perhaps for the purposes of adaptation or attention.

Consideration of the circuits involved in these connections may provide us with clues concerning the functional anatomy. Although our results do not rule out indirect connections through the lateral geniculate nucleus (LGN) or other cortical areas receiving input from area 18, the simplest explanation is probably the interruption of a direct corticocortical projection from area 18 to area 17, such as those in the upper layers (Henry et al. 1991; Mignard and Malpeli 1991). Decreased responses in area 17 cells are easy to imagine as the loss of a direct excitatory projection from area 18 to area 17, and increased responses could be the result of the loss of an inhibitory connection. Because long corticocortical connections are exclusively excitatory in the visual cortex of the cat (Bullier et al. 1988; Pérez-Cerdá et al. 1996), the inhibition would presumably be exerted through a GABAergic inhibitory interneuron within area 17. If inhibitory interneurons within area 17 can account for some of our results, they could be located either in layers 2/3 or in layer 5 (thereby acting through rising collaterals to layers 2/3). Some projections from layers 2/3 of area 18 collateralize in layer 5 of area 17 (Henry et al. 1991) and inhibitory projections from layer 5 to layers 2/3 in area 17 have been described in anatomic (Kisvárday 1992) and physiological studies (Allison and Bonds 1994). GABAergic interneurons in area 17, moreover, have been found in all layers (Gabbott and Somogyi 1986).

These findings would not necessarily apply to primate cortex. In the cat, areas 17 and 18 both receive strong geniculate input (Stone and Dreher 1973), and both areas may be thus considered, in some sense, as primary visual cortex (Tretter et al. 1975). Primate area 18 receives LGN input only from the interlaminar zones of the geniculate (Bullier and Kennedy 1983), so that feedback connections from area 18 to area 17 in the monkey may play a different role than in the cat. In the

squirrel monkey, Sandell and Schiller (1982) found that most area 17 cells showed decreased visual responses when area 18 was reversibly cooled, although a few cells became more active. Bullier et al. (1996) similarly reported in the cynomolgus monkey that, when area 18 had been inactivated by GABA, area 17 cells showed decreased or unchanged visual responses in the center of the classical receptive field, but increased responses in the region surrounding it. These results have been strengthened by recent findings in areas V1, V2, and V3 following area MT inactivation (Hupé et al. 1998).

Retinotopic relationship between area 18 and area 17

As expected from the retinotopic specificity of anatomic feedback connections (Salin et al. 1992), previous physiological studies have reported a functional projection from area 18 cells to area 17 cells with a similar retinotopy (Alonso et al. 1993b; Bullier et al. 1988; Salin et al. 1992, 1995). Our results show that the area 17 cells affected by the blockade tended to have receptive fields overlapped to a greater extent by the receptive fields in area 18 than those area 17 cells unaffected
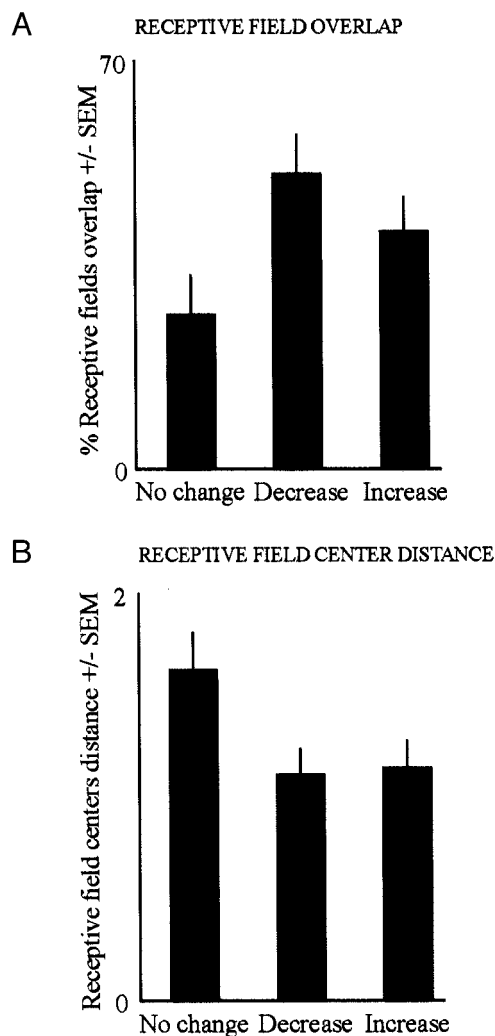

FIG. 11. Retinotopic location and effects of area 18 blockade. A: percentage of receptive fields overlap vs. type of effect: No change, Decrease and Increase. B: distance between receptive field centers in areas 17 and 18 vs. type of effect.

by the blockade (Fig. 11*A*). We also found that the distance between the receptive field centers of area 17 and area 18 tended to be smaller in cells affected by the blockade (Fig. 11*B*). Although the cell we recorded from in area 18 was probably in the center of the blocked region, many other cells were presumably inactivated, and the receptive fields from the entire population of blockaded cells most likely scattered to some extent with respect to the one we mapped, so we must consider these measures approximate.

Role of feedback connections from area 18 to area 17

In the light of anatomic evidence suggesting separate feedback pathways from area 18 to area 17 (Henry et al. 1991), the complex relationship between the two areas might be better understood by focal blockade experiments restricted to superficial or deep layers, rather than by global inactivation studies. We have found some properties of these two pathways, the superficial and the deep, we consider similar: blockade of area 18 layers 2/3 resulted in increased responses in some area 17 layers 2/3 cells and decreased responses in others, in agreement with the results reported in layer 5 (Alonso et al. 1993b).

Other properties were found to differ between superficial and deep pathways. In the original observations in cat area 17, Hubel and Wiesel (1962) suggested that the orientation selectivity of simple cells was the result of the alignment of receptive fields from afferent inputs from lateral geniculate cells. Although some studies have pointed toward local inhibition within cortex as important to generating or sharpening orientation selectivity (Bishop et al. 1971; Blakemore and Tobin 1972; Bonds 1989; Eysel et al. 1990; Crook et al. 1991; Sillito 1975; Volgushev et al. 1996), other evidence seems to run counter to this suggestion (Ferster et al. 1996; Reid and Alonso 1995). Previous work on the projections from layer 5 to layer 5 suggests that area 18 can significantly alter the bandwidth of orientation tuning curves in area 17 cells. Alonso et al. (1993b) reported that 46% of area 17 layer 5 cells changed their half-bandwidths during area 18 blockade (22% cells broadening and 24% cells sharpening their tuning curves). We have examined this possibility for the layers 2/3 projections and found no changes in orientation preference and relative lack of change in orientation bandwidth of area 17 cells.

It would not be surprising if area 18 blockade were to affect the velocity preferences of cells in area 17. In the cat, as already mentioned, cortical areas 17 and 18 receive parallel geniculate inputs. Area 17 has a major input from LGN X cells, and in a lesser extent from Y cells, whereas area 18 receives exclusively Y cell input (Ferster 1990a,b; Stone and Dreher 1973). Several characteristics of cortical cells may thus be determined by these afferents (Ferster and Jagadeesh 1991; Stone et al. 1979): Y cells respond better to higher velocity stimuli than X cells (Cleland et al. 1971), and area 18 cells similarly have an average preference for higher velocity stimuli than cells in area 17 (Tretter et al. 1975). Alonso et al. (1993a) showed that area 18 layer 5 blockade could reveal responses to high velocity stimuli in area 17 layer 5 cells, to which they were normally unresponsive. In the present study we never observed that effect: our results instead show changes in response magnitude in most or all the velocities that area 17 cells were responsive to before area 18 blockade. Although it is possible that these differences between layer 5 and layers 2/3

results are due to the different methods involved in both studies (i.e., lidocaine vs. GABA blockade), they could reflect a different functional role for the projections from area 18 at these two different levels. Thus, although both layer 5 and layer 3 pathways from area 18 seem to be involved in the modification of area 17 cells responses, the mechanisms involved and their perceptual implications could be different.

Our results show that area 18 layers 2/3 affect the responses of cells in area 17 layers 2/3 to stimuli of different orientations and velocities without fundamentally altering their specificity. These enhancements and decreases in the cells' responsiveness may suggest some kind of gain modulation from area 18 to area 17 superficial layers. Although the role of such modulation in our visual perception remains unclear, such effects could be part of a mechanism of attention or adaptation.

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