Feedback from V1 and inhibition from beyond the classical receptive field modulates the responses of neurons in the primate lateral geniculate nucleus

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Abstract

It is well established that the responses of neurons in the lateral geniculate nucleus (LGN) can be modulated by feedback from visual cortex, but it is still unclear how cortico-geniculate afferents regulate the flow of visual information to the cortex in the primate. Here we report the effects, on the gain of LGN neurons, of differentially stimulating the extraclassical receptive field, with feedback from the striate cortex intact or inactivated in the marmoset monkey, *Callithrix jacchus*. A horizontally oriented grating of optimal size, spatial frequency, and temporal frequency was presented to the classical receptive field. The grating varied in contrast (range: 0–1) from trial to trial, and was presented alone, or surrounded by a grating of the same or orthogonal orientation, contained within either a larger annular field, or flanks oriented either horizontally or vertically. V1 was ablated to inactivate cortico-geniculate feedback. The maximum firing rate of LGN neurons was greater with V1 intact, but was reduced by visually stimulating beyond the classical receptive field. Large horizontal or vertical annular gratings were most effective in reducing the maximum firing rate of LGN neurons. Magnocellular neurons were most susceptible to this inhibition from beyond the classical receptive field. Extraclassical inhibition was less effective with V1 ablated. We conclude that inhibition from beyond the classical receptive field reduces the excitatory influence of V1 in the LGN. The net balance between cortico-geniculate excitation and inhibition from beyond the classical receptive field is one mechanism by which signals relayed from the retina to V1 are controlled.

Keywords: Marmoset, Cortico-geniculate feedback, Gain, Context

Introduction

Feedback is a pervasive feature of the architecture of the visual system. At most levels of the visual system structures are reciprocally connected (Felleman & Van Essen, 1991). The first station in the mammalian visual system to receive feedback projections is the lateral geniculate nucleus (LGN). The LGN receives topographic feedback, primarily from V1 in the primate (Spatz & Erdmann, 1974; Fitzpatrick et al., 1994), and from areas 17, 18, and 19 in the cat (Robson, 1983, 1984; Sherman & Koch, 1986, 1998; Katz, 1987).

Physiological studies have found that cortico-geniculate feedback both facilitates and inhibits the relay of retinal information to the cortex (Hull, 1968; Kalil & Chase, 1970; Singer, 1977; Tsumoto et al., 1978; Gulyás et al., 1990; Cudeiro & Sillito, 1996; Marrocco et al., 1996; Wörgötter et al., 1998; Murphy et al., 1999; Cudeiro et al., 2000). Visual properties of LGN neurons can be

shaped by cortico-geniculate feedback. For example, length tuning (Murphy & Sillito, 1987), spatial structure (Marrocco & McClurkin, 1985), stimulus-linked synchronization of relay cells (Sillito et al., 1994), after-effects of adaptation (Cudeiro et al., 2000), and binocular interactions (Schmielau & Singer, 1977) in the LGN are modified by cortico-geniculate feedback. Despite the wide range of functions known to be influenced by the cortico-geniculate projection, very little is known about how the feedback projection from V1 to the LGN in the primate modulates the flow of information to the cortex.

A recent study in the macaque demonstrated that cortico-geniculate afferents increased the gain of neurons in the LGN when the classical receptive field was stimulated (Przybyszewski et al., 2000). Gain control is certainly one mechanism by which cortico-geniculate afferents could regulate the relay of visual information through the LGN to the cortex (Singer, 1977; Sherman & Koch, 1986; Koch, 1987). Solomon et al. (2002) found that visual stimulation beyond the classical receptive field reduced both gain and peak sensitivity of primate LGN neurons (Solomon et al., 2002). But they did not test whether inhibition from beyond the classical receptive field depended on the cortico-geniculate projection.

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Visual stimulation beyond the classical receptive field typically inhibits the responses of LGN neurons (Allman et al., 1985; Molotchnikoff & Cérat, 1992; Sillito et al., 1993; Cudeiro & Sillito, 1996; Felisberti & Derrington, 2001; Solomon et al., 2002). In cats, inhibition from beyond the classical receptive field in the LGN is sensitive to the orientation alignment of stimuli inside and outside the receptive field (Sillito et al., 1993; Cudeiro & Sillito, 1996). In marmosets, magnocellular neurons are much more sensitive to inhibition from beyond the classical receptive field than parvocellular or koniocellular neurons, and orientation has less impact than in cats on the level of inhibition (Solomon et al., 2002).

Here we test the hypothesis that, in the LGN, gain control by stimuli beyond the classical receptive field depends on the feedback projection from V1. We show how, with and without V1 intact, the orientation and location of stimuli beyond the classical receptive field modulate the responses of magnocellular and parvocellular neurons in the LGN of the marmoset (*Callithrix jacchus*), a diurnal New-World monkey. A preliminary report of these results has been published elsewhere (Webb et al., 2001).

Methods

We recorded extracellular responses of single neurons in the LGN, with feedback from the striate cortex present or absent in eight anesthetized and paralyzed marmosets (New-World monkey, *Callithrix jacchus*). All preparatory and surgical procedures were in accordance with the guidelines of the UK Animals (Scientific Procedures) Act of 1986.

Surgical preparation

Saffan (Alphadalone/Alphaxalone acetate; 1.5 ml/kg i.m.) was administered to induce anesthesia. Depth of anesthesia was monitored by frequently testing for the presence of a leg flexion reflex, and if this were present, additional doses of Saffan were administered. The lateral tail veins were cannulated, and the trachea was cannulated so the animal could be artificially respired. In males the urethra was catheterized.

The animal was mounted in a stereotaxic frame and its head positioned with a bite bar, eyehooks set into the infraorbital foramen, and ear bars coated in lidocaine hydrochloride gel. The head was held in position by a head post cemented to the frontal bone with dental acrylic, and a craniotomy was performed to gain access to the right LGN .

Surgical anesthesia was maintained with N_2O (70%), O_2 (30%), and a continuous intravenous infusion of fentanyl citrate (20 $\mu g \cdot kg^{-1} \cdot h^{-1}$) in a saline-glucose solution (1.5 ml/kg/h). Vecuronium bromide (0.1 $mg \cdot kg^{-1} \cdot h^{-1}$) was included in the infusion to induce paralysis of the skeletal muscles. The animal was artificially respired and respiration was adjusted to maintain the peak percentage of CO_2 in the expired air at between 3.5 and 5%. Body temperature was maintained close to 37.5°C by an electric blanket controlled by a rectal thermistor. Electrocardiogram and electroencephalogram activity were monitored continuously throughout the experiment. Supplementary anesthesia (halothane or fluothane) was given if necessary.

Optics

The pupils were dilated with atropine sulphate and the eyes were protected by gas-permeable contact lenses of zero-added power.

The refractive error of each eye was corrected with miniature spectacle lenses that optimized the response of an isolated neuron to a high spatial-frequency sine-wave grating. The optic disk and fovea of each eye were plotted on a tangent screen 57 cm in front of the animal with a reversing opthalmoscope.

Physiological recording

The retinotopic mapping study of White et al. (1998) was used as a guide for penetrations in the LGN. Extracellular responses were recorded from neurons in the right LGN with glass-insulated tungsten electrodes (Merrill & Ainsworth, 1972). The signal was amplified, band-pass filtered, and then sampled and time-stamped with a resolution of 100 μs by a digital signal processor housed in the computer. To discriminate the signal of an individual neuron from the background activity, a template of the shape of action potential traces was constructed, and all incoming spikes were matched to this template using a goodness-of-fit criterion.

Visual stimuli

Stimuli were generated by a Macintosh computer using a Radius 10-bit graphics card and presented initially using a video data projector on a tangent projection screen subtending approximately 87 deg × 67 deg at a viewing distance of 57 cm. Receptive fields were mapped with sinusoidal gratings and then positioned on the center of a CRT display monitor with a front-surfaced mirror. The CRT display (Sony Model No. GDM 200PST) subtended 15.5 deg × 11.5 deg at a viewing distance of 114 cm, had a mean luminance of approximately 50 cd/m^2, and a frame rate of 120 Hz. The display nonlinearity was corrected using a lookup table. Contrast of visual stimuli was specified by Michelson contrast $(L_{max} - L_{min})/(L_{max} + L_{min})$.

A neuron's polarity (on or off-center) was determined by comparing its response to bright and dark spots. Its spatial- and temporal-frequency tuning and optimal stimulus size were measured with drifting sinusoidal gratings. The optimal value for each of these measures was used in subsequent experimental tests. To ensure that extraclassical stimuli did not stimulate the classical receptive field, an annular patch of drifting grating was presented to the classical receptive field and recenterd and/or resized until no response was evoked from the neuron.

In the experiment reported here, a drifting horizontally oriented sinusoidal grating was presented to the classical receptive field for 500 ms. The grating varied in contrast, in the range 0–1, and was presented alone, or surrounded by a drifting grating of the same or orthogonal orientation contained within either (1) a larger annular field which was 10 deg × 10 deg in size, (2) horizontally oriented flanks which were the length of the receptive field and 10 deg wide, or (3) vertically oriented flanks which were the width of the receptive field and 10 deg in length. The spatial phase of extraclassical stimuli was the same as the stimulus presented to the CRF.

The different conditions were presented 60 times (10 repetitions of 6 contrast levels of the grating presented to the CRF) in an interleaved fashion with interstimulus intervals of 500 ms.

Inactivation of cortico-geniculate feedback

Supplementary anesthesia (fluothane) was given during the lesion surgery. In four animals, an aspiration lesion of the striate cortex was made to inactivate the feedback to the LGN from the striate

cortex. In three individuals, the whole extent of the striate cortex was ablated. In one individual, only cortical tissue representing the central 5 deg of the visual field was ablated. To gain access to the striate cortex, a cranial bone flap was made. The flap extended anteriorly from the inion approximately 8 mm, and laterally from the midline as far as necessary to expose the lateral convexity. A dural flap was reflected to expose the surface of the cortex, and the tissue was ablated by aspiration. Recordings were made in the LGN immediately after V1 had been ablated.

Histology and track tracing

At the conclusion of each experiment, an intravenous overdose of pentobarbitone (Sagatal; 60 μg/ml) was given. Once electrocardiogram, electroencephalogram, and CO_2 traces became flat, animals were perfused through the heart, initially with phosphate buffer, and then with 4% formaldahyde. The brain was removed and stored in a 30% sucrose solution until it sank. It was sectioned (at 60 μm) with a freezing microtome; sections were mounted and stained with cresyl violet.

Microlesions (5 μA for 5 s electrode negative) were made at different depths on each penetration. These, and the sequence of changes in ocular dominance, were used to reconstruct each electrode track and assign cells to either the parvocellular, koniocellular, or magnocellular layers.

Data analysis

The dependent measure used at all stages of the data analysis (unless otherwise stated) was the response amplitude at the fundamental frequency of the drifting sinusoidal grating. Changes in higher harmonics were not considered here. To quantify the differential modulation of the response *versus* contrast function by stimuli beyond the classical receptive field, the response of a neuron to each stimulus condition was compared by fitting the Michaelis-Menten equation to each cell's response *versus* contrast function by minimizing the squared error. The equation is

$$R = R_{max} c^n/(c^n + c_{50}{}^n) + M. \qquad (1)$$

R_{max} is the maximum attainable response, c_{50} is the contrast at which the response reached half its maximum value, n indicates the steepness of the curve, and M is the spontaneous firing rate.

Results

The data described here were obtained from 19 neurons (10 on-center, 9 off-center) in the parvocellular (P) layers and 15 neurons (5 on-center, 10 off-center) in the magnocellular (M) layers in the right LGN of the marmoset, recorded with the striate cortex intact. With the striate cortex ablated, data were obtained from 16 neurons (5 on-center, 11 off-center) in the P layers and 13 neurons (4 on-center, 9 off-center) in the M layers. Cells were recorded at eccentricities between 4.3 and 15.9 deg with feedback intact, and between 0.8 and 8.5 deg with feedback inactivated.

In what follows, classical receptive field refers to both the "center" and "surround" "on" and "off" regions of a LGN receptive field, whereas extraclassical refers to visual space beyond the classical receptive field. Fig. 1 shows typical responses of a LGN neuron (magnocellular on-center) with V1 intact (left column), and a LGN neur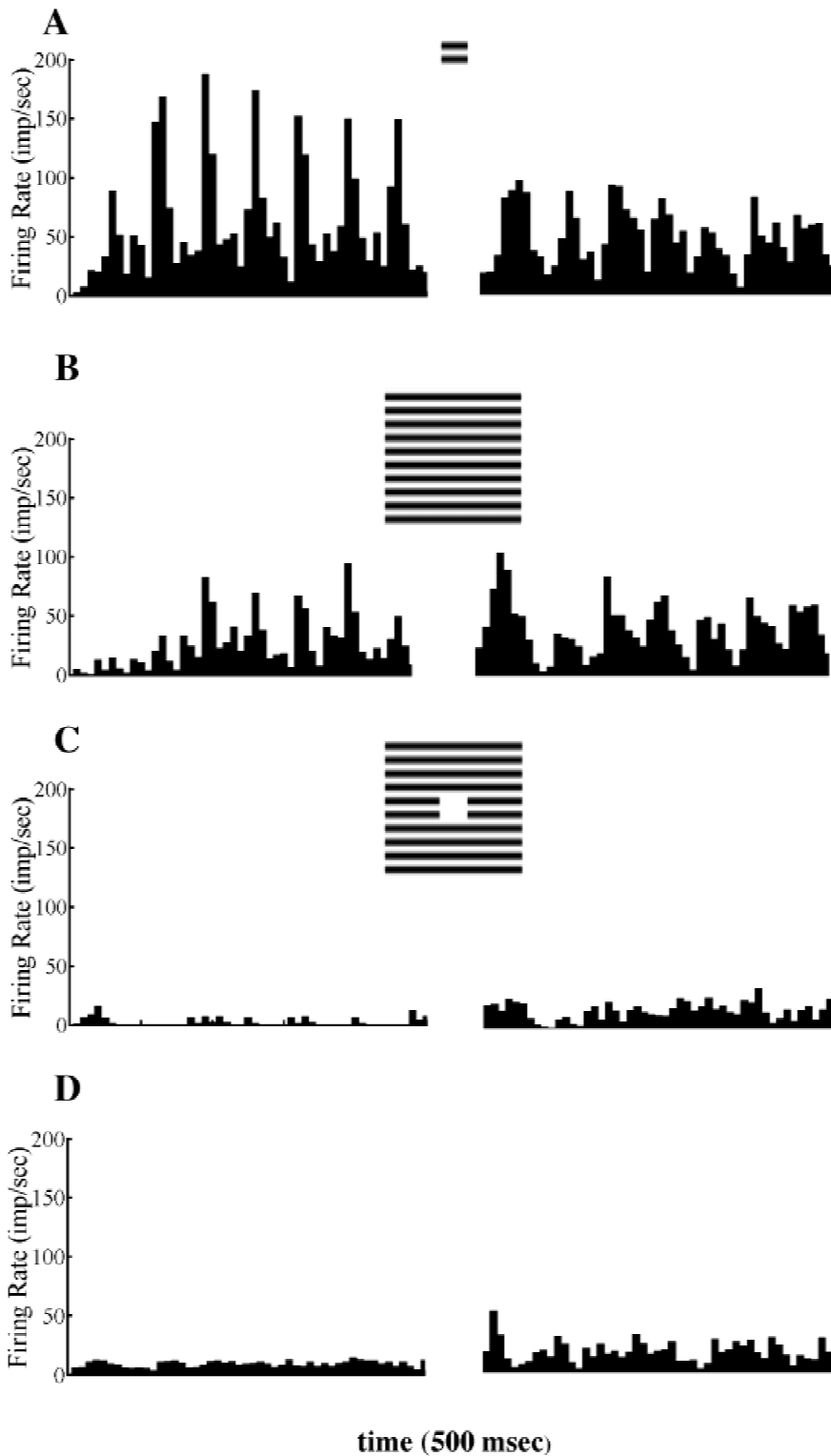on (magnocellular on-center) with V1 ablated (right column). With V1 intact, the response to a grating covering the classical receptive field (Fig. 1A, left) is suppressed by the addition of a large annular grating beyond the classical receptive field (Fig. 1B, left). The spontaneous activity (Fig. 1D, left) is slightly suppressed when the annular grating is presented alone (Fig. 1C, left). However, the suppression of evoked activity is much greater (approximately 100 impulses/s) than the suppression of the spontaneous activity. With V1 ablated, the response of a LGN neuron to a grating covering its classical receptive field was lower (Fig. 1A, right) than in the example recorded with V1 intact, but the degree of suppression caused by the presence of an annular grating beyond the classical receptive field was much less (Fig. 1B, right). The spontaneous activity (Fig. 1D, right) was also less affected by extraclassical stimulation (Fig. 1C, right) compared to when V1 was intact.

Cortical feedback and stimulation beyond the classical receptive field

How does feedback from V1 and extraclassical stimulation modulate the activity of LGN neurons? To investigate the influence that feedback from the striate cortex has over extraclassical interactions in the LGN, we measured the modulated response of LGN neurons to gratings of a range of different contrasts, in the presence or absence of extraclassical stimuli, with V1 either intact or ablated. To characterize how different extraclassical stimuli modulated the activity of LGN neurons, the Michaelis-Menten equation was fitted to response *versus* contrast functions obtained under seven stimulus conditions (Fig. 2A). We estimated values of each of the parameters R_{max}, c_{50}, and n that were required to produce curves that fit the neuron's response *versus* contrast function under the seven stimulus conditions. For each neuron, the seven curves were fit simultaneously, and two parameters were constrained to have the same value for all seven curves, while the third parameter and M were allowed to vary from curve to curve. Good fits could be obtained by allowing any of the parameters to vary. We chose to use R_{max} to characterize changes in gain because variations in R_{max} are easiest to interpret. They simply scale the whole curve up or down, changing the gain without changing the slope. The best fits (fraction of variance explained > 90 %) were obtained in 13/19 P neurons and 12/15 M neurons with feedback from V1 intact, and 13/16 P neurons and 10/13 M neurons with feedback from V1 inactivated. Data from neurons not meeting our curve fit criterion were excluded from further analysis. Hereafter the analysis is confined to R_{max} values obtained from these constrained curve fits.

Figs. 2B and 2C are examples of such constrained fits to data obtained under the seven stimulus conditions from a P and an M cell, respectively. All extraclassical stimuli reduced the evoked activity of LGN neurons. In the P cell, R_{max} was reduced by up to 73%, and in the M cell by up to 67%. The size of extraclassical stimuli was the most important factor determining the degree of reduction in response. Flanking stimuli at different locations reduced the response of these neurons, but the largest extraclassical stimuli produced the greatest reduction in response. The orientation of extraclassical stimuli did not appear to be important to the reduction in response observed here.

Figs. 2D and 2E are examples of constrained curve fits to data obtained from a P and M cell, with R_{max} allowed to vary, and with the striate cortex ablated. In both cases, removing the cortex considerably reduced the extraclassical reduction in response observed when feedback was intact.

Fig. 1. Extraclassical inhibition in LGN cells, with V1 intact or ablated. Each row shows the stimulus configuration above a peristimulus time histogram. The left column is the response of a magnocellular on-center cell, recorded when V1 was intact, to each stimulus configuration. The right column is the response of a magnocellular on-center cell, recorded after V1 had been ablated, to each stimulus configuration. The example response to a grating of optimal spatial and temporal frequency restricted to the classical receptive field (A, left panel) is smaller in the neuron recorded with V1 ablated (A, right panel). The response of the neuron recorded when V1 was intact is reduced by the presence of large, high-contrast annulus grating outside the classical receptive field (B, left panel). With V1 ablated, the degree of suppression of the evoked activity caused by the presence of an annular grating beyond the classical receptive field was much less (B, right panel) than in the example when V1 was intact. With V1 ablated, the degree of suppression of the spontaneous activity caused by the presence of an annular grating beyond the classical receptive field was less (C, right panel) than in the example when V1 was intact (C, left panel). Left panel of D shows the spontaneous activity with V1 intact; right panel of D shows the spontaneous activity after V1 was ablated.

To determine whether a reduction in R_{max}, in response to extraclassical stimulation, was characteristic of the full sample of neurons described here, we plotted the best-fitting R_{max} values for the grating-alone condition against the best-fitting R_{max} values for each of the extraclassical conditions, for each neuron. Fitted values of R_{max} were outside the normal physiological range (>500 impulses/s) in three neurons, when the cortex was intact, and in three neurons when it was ablated. These neurons were excluded from further analysis.

Figs. 3A–3F show examples in which the R_{max} values for each neuron for the grating-alone condition are plotted against the R_{max} values for each of the grating-alone and extraclassical stimulus conditions, with V1 intact. Data points below the diagonal indicate that R_{max} in response to the grating stimulating the receptive field

A

B

C

D

E
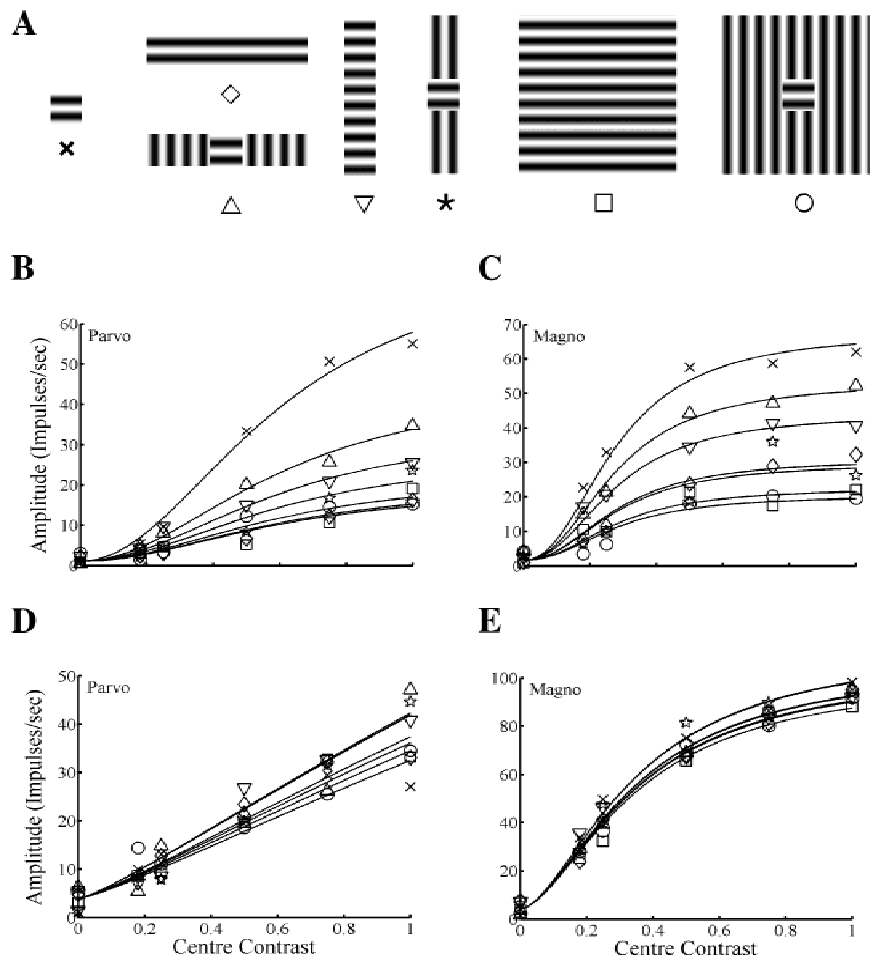
Fig. 2. Effects of extraclassical stimulation on the response *versus* contrast functions of LGN cells, with V1 intact or ablated. A: A schematic illustration of each stimulus configuration. In each example (B–E), the seven curves are best-fitting results of Eqn. (1), with the parameters fit simultaneously with the following constraints. Parameters c_{50} and n were constrained to have the same value for all seven curves while R_{max} and M were allowed to vary from curve to curve. The gain of both a parvocellular on-center neuron (B) and a magnocellular on-center neuron (C) is reduced by extraclassical stimulation. In both cases the size, rather than the orientation of extraclassical stimuli, is most important for the degree of gain reduction. After V1 was ablated, the extraclassical reduction in gain was substantially less in both a parvocellular on-center (D) and a magnocellular on-center neuron (E).

was increased by extraclassical stimulation. Data points above the diagonal indicate that R_{max} in response to the grating stimulating the receptive field was reduced by extraclassical stimulation. In the majority of cells, R_{max} was reduced by the presence of a large annular grating of either orientation (Figs. 3C & 3F). The reduction in R_{max} appears to be most marked in magnocellular cells. Flanking stimuli of either orientation also reduced R_{max} (Figs. 3A, 3B, 3D, & 3E), but not to the same extent as large annular gratings.

Most of the extraclassical stimuli used here produced reductions in R_{max}. Figs. 3G–3L show that ablating V1 considerably reduces the reduction in R_{max} caused by extraclassical stimulation when the cortex was intact. Under all extraclassical stimulus conditions, the reduction in R_{max} when V1 was intact is either reduced or abolished in neurons after V1 was ablated.

*Extraclassical inhibition in neurons from different lamina of different polarity*

Figs. 3A–3F give the impression that magnocellular neurons were more susceptible to extraclassical inhibition than parvocellular neurons. To test this idea, we calculated a R_{max} ratio [(R_{max} with extraclassical stimulation − R_{max} with receptive-field stimulation alone)/R_{max} with receptive-field stimulation alone]. A ratio of 0 indicates no effect of extraclassical stimulation, a positive ratio indicates extraclassical facilitation, and a negative ratio indicates extraclassical inhibition.

The mean R_{max} ratio for each extraclassical stimulus, for parvocellular and magnocellular cells recorded with V1 intact, is plotted in Fig. 4A. To perform statistics, we grouped these data by grating orientation (horizontal or vertical) and cell type (magnocellular or parvocellular). A mixed ANOVA revealed that extraclassical horizontal gratings (mean −0.28; S.E.M. ± 0.03) reduced the R_{max} ratio by a larger degree than extraclassical vertical gratings (−0.23 ± 0.03) ($P < 0.01$). Extraclassical stimuli reduced the R_{max} ratio in M cells (−0.35 ± 0.03) by a larger degree than in P cells (−0.15 ± 0.03) ($P < 0.001$).

The mean R_{max} ratio for each extraclassical stimulus, for on-center and off-center cells, is plotted in Fig. 4B. These data were grouped by grating orientation and polarity (on- or off-center). A mixed ANOVA revealed that extraclassical stimuli of either orientation were not any more effective in reducing the R_{max} ratio in on-center cells (−0.27 ± 0.04) than they were in off-center cells (0.23 ±0.04).

Cortico-geniculate excitation and extraclassical inhibition

Przybyszewski et al. (2000) found that the gain of parvocellular and magnocellular neurons is increased by feedback from the striate cortex in the macaque. Unlike the stimulus paradigm used here, in their experiments they stimulated the classical receptive field but did not explore the effects of extraclassical stimuli. These differences in experimental design raise an interesting question: is
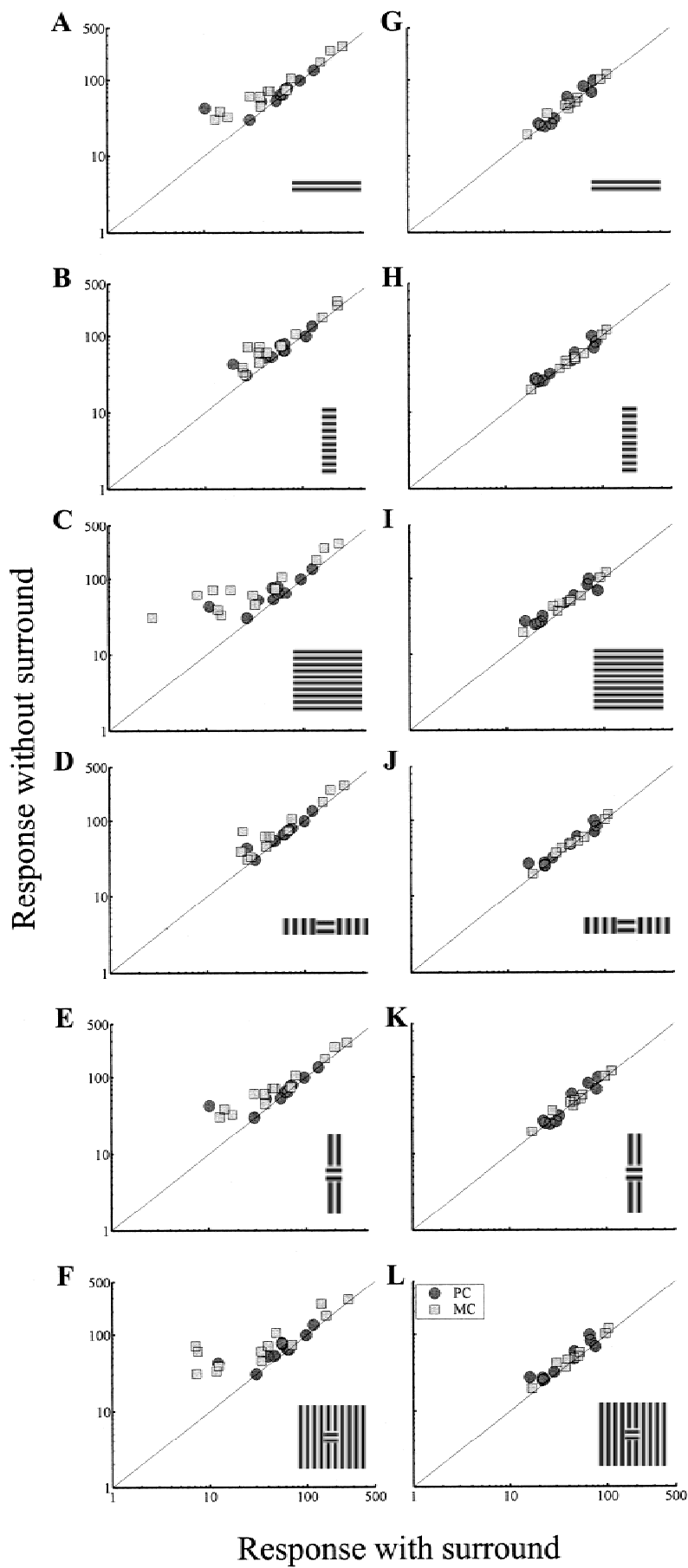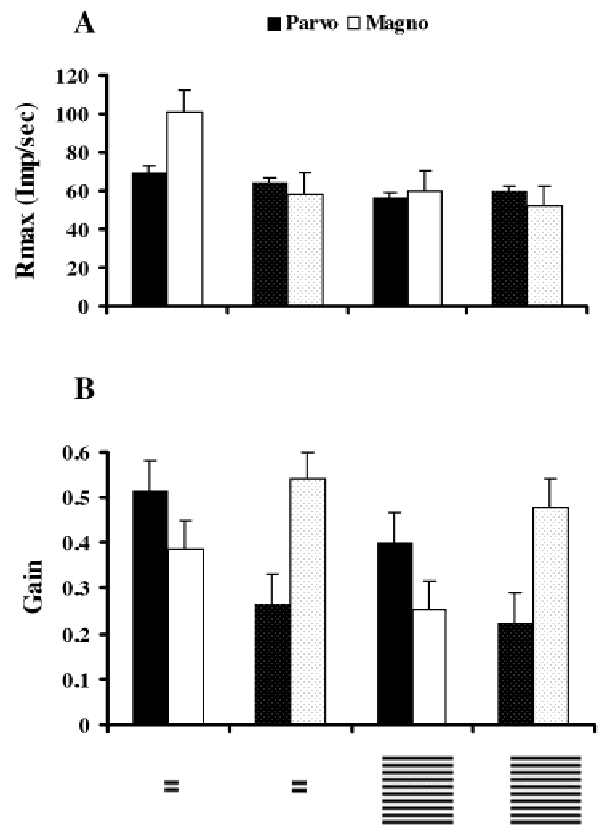
Fig. 3. Effects of extraclassical stimulation on the R_{max} of LGN neurons to stimulation of the classical receptive field, with V1 intact or ablated. The best-fitting R_{max} values for the grating-alone condition are plotted against the best-fitting R_{max} values for each of the extraclassical stimulus conditions, for each neuron when V1 was intact (A–F), and when it was ablated (G–L). All extraclassical reduced the R_{max} of a small proportion of neurons, but large extraclassical stimuli of either orientation reduced R_{max} by the greatest degree. After V1 was removed, the inhibitory effects of extraclassical stimuli were substantially diminished. PC: parvocellular neurons; and MC: magnocellular neurons.
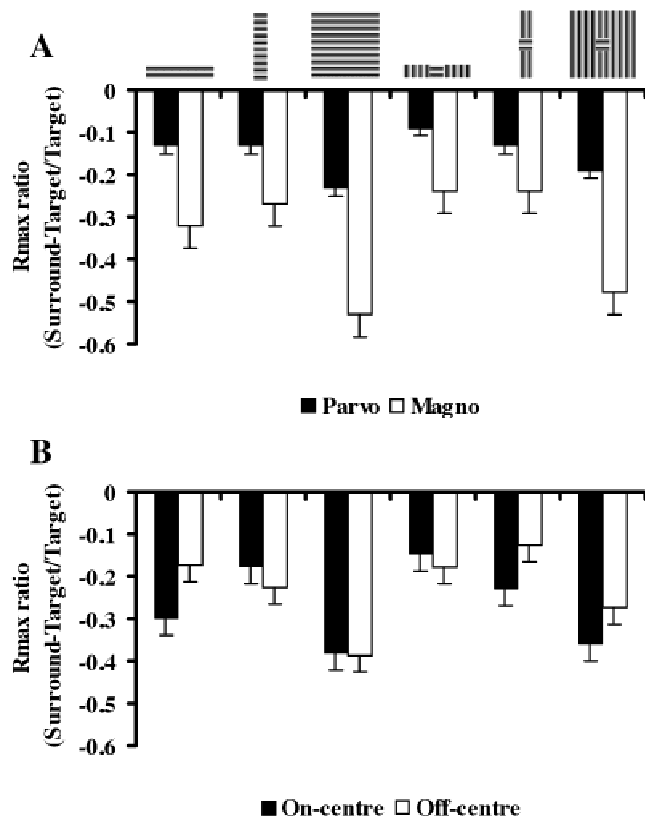
Fig. 4. R_{max} ratio [(R_{max} with extraclassical stimulation − R_{max} with receptive-field stimulation alone)/R_{max} with receptive-field stimulation alone] in parvocellular and magnocellular neurons, and on-center and off-center neurons with V1 intact. The R_{max} ratio of magnocellular neurons was reduced to a greater degree than that of parvocellular neurons by extraclassical stimulation (A). There were no differences between on-center and off-center cells in the degree of reduction of the R_{max} ratio by extraclassical stimuli (B).

Fig. 5. Relative effects of excitatory feedback from V1 and extraclassical inhibition on the R_{max} and response per percent contrast of LGN neurons. A: The best-fitting R_{max} values for the grating-alone condition and grating-alone + horizontal annulus grating are plotted when the cortex was intact (open bars) and ablated (stippled bars). When visual stimulation was restricted to only the classical receptive field of LGN neurons and V1 was intact, the R_{max} was greater than when V1 was ablated. Extraclassical stimulation with V1 intact reduced the R_{max} to the same value as was obtained with a V1 lesion. B: The response per percent contrast for the grating-alone condition and grating-alone + horizontal annulus grating are plotted when the cortex was intact (open bars) and ablated (stippled bars). The impression given by this plot that the gain of magnocellular neurons is increased and the gain of parvocellular neurons is reduced after V1 was ablated is not borne out by the statistics reported in the main text.

the reduced extraclassical inhibition seen here with the cortex ablated caused by removal of excitatory or of inhibitory cortical influences on the LGN?

Two possibilities are considered. First, ablating V1 disrupts excitatory cortico-geniculate interactions at the classical receptive field, but not extraclassical inhibition. Second, ablating V1 disrupts both excitatory interactions at the classical receptive field and extraclassical inhibition. To answer this question, we consider only the comparison between the mean R_{max} obtained from stimulating the classical receptive field alone, and mean R_{max} obtained from stimulating both the classical receptive field and beyond the classical receptive field with a horizontal annular grating, when the cortex was intact and ablated. Fig. 5A indicates that when the cortex is intact and only the classical receptive field is stimulated, extraclassical stimulation and ablating V1 have equivalent effects on R_{max}. A mixed ANOVA (stimulus *vs.* cortical inactivation *vs.* cell type) revealed a significant main effect of stimulus ($P <$ 0.001), a significant two-way interaction between stimulus and cortical inactivation ($P < 0.001$) and a significant three-way interaction ($P < 0.01$). These results confirm the impression given by Fig. 5A. Ablating V1 reduced the mean R_{max} of magnocellular neurons to stimulation of the classical receptive field by 42.60 impulses/s, and extraclassical stimulation reduced the mean

R_{max} of magnocellular neurons by a comparable amount (41.50 impulses/s).

The maximum obtainable firing rate is not typically used as measure of gain. The response/percent contrast is a more widely used measure of gain. For comparison, therefore, we conducted the same analysis as above on this measure of gain [the modulated firing rate obtained at 5% contrast − spontaneous firing rate/5]. These values were measured from the curve fits to the data. Fig. 5B gives the impression that the gain of magnocellular neurons is increased after V1 was ablated, regardless of whether there is an extraclassical stimulus present or not. The gain of parvocellular neurons appears to be reduced to an equivalent degree by extraclassical stimulation and ablating V1. However, the statistics do not bear this impression out, due to the larger variability in the data. Using this measure of gain, the only effect that remains statistically significant is a reduction in the gain of LGN neurons of 0.9 by stimulating beyond the classical receptive field ($P < 0.001$).

Discussion

We found that stimulating beyond the classical receptive field reduced the gain of LGN neurons in anesthetized marmosets. Stimulating large areas beyond the classical receptive field with horizontal or vertical stimuli was most effective in reducing the gain of LGN neurons. The reduction in gain was most pronounced in magnocellular neurons. The effects that ablating V1 had on the gain of LGN neurons depended on how gain was measured. Both the maximum obtainable firing rate of LGN neurons and the inhibitory influence of extraclassical stimuli were reduced after ablating V1. However, ablating V1 had no statistically significant effect on the response per percent contrast.

These findings raise three questions. First, how do these cortico-geniculate and extraclassical effects in the marmoset compare to similar work in the cat and macaque? Second, what is their anatomical mechanism? Third, what is the functional significance of extraclassical inhibition and cortico-geniculate excitation in the LGN?

Cortico-geniculate excitation and extraclassical inhibition in the LGN

Przybyszewski et al. (2000) demonstrated, in the macaque, that the gain of LGN neurons was increased by feedback from V1, when only the classical receptive field was stimulated. Except at low contrasts in magnocellular neurons, they found that the gain of both parvocellular and magnocellular neurons was increased by feedback from V1. Contrary to these results, we found no effect on the gain of LGN neurons after ablating V1. This discrepancy may be explained by differences in the regimes used to stimulate the classical receptive field. For example, Przybyszewski and his colleagues changed contrast in logarithmic steps, whereas we changed contrast in linear steps. This seems an unlikely explanation, however, because in both studies the estimates of gain are based on curve fits to the full set of responses. Thus, differences in sampling are unlikely to contribute significantly to the discrepancy in results, provided the curve fits are adequate.

A more likely explanation, however, is that Przybyszewski and his colleagues made a direct comparison of changes in the activity of the same LGN neuron before, during, and after temporary inactivation of V1, whereas we made a more indirect comparison across animals. There are several limitations of the nonreversible inactivation regime we have employed here. For example, it is not possible to compare the responses of the same neuron before, during, and after inactivation, or to verify the integrity of the cortex after inactivation. It may be that comparisons between animals with V1 intact and V1 ablated reveal only a general reduction in the activity of LGN neurons of the sort that we report here. More subtle changes in responsiveness, such as modulations in gain, may only emerge when the properties of the same LGN cell can be compared before and during temporary inactivation of V1 as in Przybyszewski et al's experiment.

Przybyszewski and his colleagues also found that the maximum obtainable firing rate was reduced in LGN neurons during inactivation of V1. We confirm this finding in magnocellular neurons in the marmoset, and extend it by showing results that suggest that the excitatory influence of the cortex in the LGN is blocked by stimulating beyond the classical receptive field. We used only stimuli that were modulated in luminance, and it may be that chromatic contrast is more effective for activating the feedback projection from V1 to parvocellular neurons (Przybyszewski et al., 2000).

Parvocellular neurons were also less susceptible than magnocellular neurons to inhibition from beyond the classical receptive field. Solomon et al. (2002) also found that extraclassical interactions were predominantly inhibitory, and more pronounced in the magnocellular than in the parvocellular pathway. They showed that extraclassical inhibition was maximal at aperture sizes of 2 deg. Although we found that large (10 deg) extraclassical stimuli were most effective in reducing the gain of LGN neurons, because we did not manipulate the size of extraclassical stimuli, we cannot exclude the possibility that smaller stimuli would have produced equivalent effects.

An unresolved issue is whether the relative orientation of stimuli within and beyond the classical receptive field is important for extraclassical inhibition in the LGN. In cat LGN, extraclassical inhibition is sensitive to the relative orientation of stimuli inside and outside the classical receptive field (Sillito et al., 1993; Cudeiro et al., 2000), whereas in marmoset LGN it is not (Solomon et al., 2002). Although we found that the gain of LGN neurons was more reduced by horizontal than vertical extraclassical gratings, the mean difference was very small, and probably of little functional relevance.

Mechanisms of cortico-geniculate excitation and extraclassical inhibition

By what mechanism(s) does feedback from V1 regulate the modulation in firing rate of LGN neurons reported here? The incremental signal (increase in the maximum firing rate when V1 was intact) is probably carried by axons of pyramidal neurons in layer 6 of V1 that form direct excitatory synapses with distal dendrites of relay cells. *En route* these axons also send collaterals to neurons in the reticular nucleus of the thalamus in the primate (Orgren & Hendrickson, 1976; Symonds & Kaas, 1978; Conley & Diamond, 1990), which in turn form inhibitory synapses with the dendrites of relay cells (Harting et al., 1991; Feig et al., 1998; Bickford et al., 2000). This indirect pathway to the LGN is one route by which an inhibitory signal (reduction in the maximum firing rate by stimulating beyond the classical receptive field) could be sent. The receptive fields of cells in the reticular nucleus of the thalamus are certainly large enough (3–10 deg or more in diameter) to be activated by the extraclassical stimuli used here (Funke & Eysel, 1998).

Relay cells in the LGN also send axons to the reticular nucleus of the thalamus (Sherman & Koch, 1986, 1998). It is possible, therefore, that the recurrent projection between relay cells and interneurons in the reticular nucleus of the thalamus, modulate the reduction in maximum firing rate caused by extraclassical stimulation that we report here. The net balance between excitation and inhibition observed here in the LGN may therefore be regulated by the relative strength and timing of activation of feedback projecting axons originating in V1 and the reticular nucleus of the thalamus. It's not clear from our data, however, whether the origin of the signal to the reticular nucleus of the thalamus is the cortex or the LGN.

Functional significance of cortico-geniculate facilitation and extraclassical inhibition

It has been known for some time that cortico-geniculate feedback modulates the flow of visual information that reaches the cortex (Hull, 1968; Kalil & Chase, 1970; Singer, 1977; Tsumoto et al., 1978; Marrocco & McClurkin, 1985; Sherman & Koch, 1986;

Murphy & Sillito, 1987; Marrocco et al., 1996; Cudeiro et al., 2000). Until relatively recently, *in vivo* experimental evidence of a mechanism by which the cortex regulates the flow of visual information through the LGN was lacking. Numerous hypotheses have been offered on the subject, and many agree that a function of CG feedback is to "gate" or regulate the gain of retinal signals that reach the cortex (Singer, 1977; Sherman & Koch, 1986; Koch, 1987).

Here we demonstrate in the primate that the maximum rate of retinal signals reaching V1 appears to depend on the net balance of excitation from regions within the classical receptive field provided by feedback from V1, and inhibition from regions beyond the classical receptive field. The greater susceptibility of magnocellular neurons to excitatory input from V1 and to inhibition from outside the classical receptive field suggests that one function of these mechanisms may be to increase the rate of retinal signals at particular locations in the visual field, and suppress signals at other locations. Thus, retinal signals at specific locations in the visual field would receive selective access to V1. The lack of stimulus selectivity beyond the classical receptive field that we, and others (Solomon et al., 2002), have found in the primate, support a more global mechanism such as this.

We have alluded to the potential that chromatic stimulation may have in activating feedback signals from V1 to parvocellular neurons. Przybyszewski et al. (2000) found that the feedback from V1 in macaques increased the gain of a small sample of parvocellular neurons, which were stimulated with gratings modulated in chromatic contrast. Future research may benefit from examining how extraclassical chromatic stimulation modulates the output of parvocellular neurons. The challenge is to establish the necessary and sufficient visual conditions under which the gain of parvocellular and magnocellular neurons are increased and decreased by cortico-geniculate feedback.

Conclusion

Feedback from V1 to the LGN in the marmoset increases the maximum firing rate of LGN neurons. A function of inhibition from outside the classical receptive field was to reduce the excitatory influence of V1 in the LGN. Both excitatory feedback from V1, and inhibition from beyond the classical receptive field, were more effective on magnocellular neurons than on parvocellular neurons. We conclude that the net balance between cortico-geniculate excitation, and inhibition from beyond the classical receptive field, is one mechanism by which the rate of signals relayed from the retina to V1 is controlled.

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