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THE BINOCULAR INPUT TO CELLS IN THE FELINE DORSAL LATERAL GENICULATE NUCLEUS (dLGN).

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SUMMARY

1. Cells in the A laminae of the dorsal lateral geniculate nucleus receive their primary innervation from either the contralateral (A) or ipsilateral (A1) eye. This paper provides evidence concerning the responses they give to visual stimulation of what is commonly regarded as the ineffective or non-dominant eye. It also examines the contribution of the corticofugal input to these responses.

2. Cells were identified and classified according to their responses to stimulation of the dominant eye receptive field. This was then occluded and the corresponding location in the non-dominant eye field stimulated by a moving bar. Out of fifty-seven cells examined forty-three (75%) gave a response to stimulation of the non-dominant eye. There was no obvious difference between the effects on X and Y cells in these experiments.

3. In most cases (thirty-seven) the response involved an inhibition of the resting discharge level, but three cells gave a mixed excitatory and inhibitory response and three a pure excitatory response. All the responses were weak and only revealed by prolonged periods of averaging (20–100 trials).

4. Ionophoretic application of the GABA antagonist *N*-methyl-bicuculline (NMB) blocked the visually elicited inhibitory effects and in most cases (twenty-seven out of thirty-two tested) revealed an excitatory response. Out of a further eight cells previously unresponsive to the non-dominant eye, NMB application revealed excitatory responses in three.

5. Increasing background discharge levels and cell excitability by ionophoretic application of either acetylcholine or the excitatory amino acid, quisqualate, did not eliminate inhibitory responses and did not reveal excitatory responses. We suggest that the visually driven non-dominant eye suppression of the background discharge involves a GABA-mediated inhibitory input which masks an underlying excitatory input.

6. An excitatory non-dominant eye response could potentially derive from the influence of the corticofugal projection. However, removal of the corticofugal input by aspiration of areas 17 and 18 did not reduce either the excitatory or the inhibitory components of the response.

7. In the absence of corticofugal input all cells tested (fourteen) exhibited a non-dominant eye response and all studied during NMB application (eleven) gave an

excitatory response. The primary effect of removing the corticofugal input appeared to involve the loss of a 'damping' influence on the excitatory and inhibitory responses, such that they were more easily revealed. The significance of these findings is discussed.

INTRODUCTION

The excitatory responses of cells in the feline dorsal lateral geniculate nucleus (dLGN) are generally considered to be strictly monocular (Hubel & Wiesel, 1961). This can be related to the sharp laminar segregation of the two retinal inputs in the dLGN (Hickey & Guillery, 1974; Bowling & Michael, 1984). Thus cells in lamina A for example receive their excitatory drive from the contralateral eye and appear superficially to be unresponsive to the ipsilateral eye. However it has been known for some time that the 'ineffective' or 'non-dominant' eye does in fact provide an inhibitory drive (Sanderson, Bishop & Darian-Smith, 1971) which can be very potent (Pape & Eysel, 1986). There is also some evidence for an excitatory input from the non-dominant eye. Schmielau & Singer (1977), utilizing a binocular stimulus protocol, observed both facilitatory and inhibitory influences deriving from the non-dominant eye input to dLGN cells, and in a small number of cases weak excitatory effects to monocular stimulation have been reported (Sanderson *et al.* 1971). Given the presence of the massive corticofugal projection to the dLGN it is hardly surprising that some dLGN cells exhibit binocular excitatory responses. The density of this direct excitatory projection to dLGN relay cells considerably exceeds that of the retinal input (Robson, 1983; Wilson, Friedlander & Sherman, 1984). It is inferred to be binocular because individual corticofugal axons have been observed to arborize in both laminae A and A1 (Guillery, 1967; Updyke, 1975; Robson, 1983; Boyapati & Henry, 1984) and because some layer VI corticofugal cells exhibit binocular responses (Gilbert 1977; Harvey 1980; Tsumoto & Suda, 1980). Taken as a whole the evidence would suggest that the majority of dLGN cells have access to a corticofugally mediated non-dominant eye facilitation. From this it is difficult to avoid the conclusion that the non-dominant eye inhibitory responses mask an underlying excitatory input.

These inhibitory responses could originate from two sources. One is the population of intrinsic inhibitory interneurones and the other, inhibitory neurones in the perigeniculate nucleus. The intrinsic inhibitory interneurones receive direct retinal input and appear to mediate a feed-forward inhibition whilst the perigeniculate cells, driven by relay cell collaterals provide a recurrent feedback inhibition (Famiglietti & Peters, 1972; Rapisardi & Miles, 1984; Wilson *et al.* 1984; Ahlsen, Lindstrom & Lo, 1985). Both groups receive corticofugal terminals and hence could be involved in binocular effects (Updyke, 1975; Ide, 1982; Montero & Singer, 1984, 1985). However there is also clear evidence to indicate that inhibitory effects can be elicited from the non-dominant eye in the absence of corticofugal feedback (Pape & Eysel, 1986), confirming the presence of subcortically mediated binocular inhibitory influences acting on dLGN cells (Suzuki & Kato, 1966; Lindstrom, 1982).

There is clearly a basis for several levels of binocular interaction in the dLGN and this could have considerable functional import. It is thus of great interest to know

whether the non-dominant eye inhibition does in fact submerge an excitatory drive. In this paper we describe experiments that demonstrate the presence of non-dominant eye excitatory responses during the blockade of inhibitory inputs acting on dLGN cells and explore the contribution of the corticofugal system to these responses. Our basic experimental approach follows evidence indicating that GABA is the inhibitory transmitter mediating the effects of the two groups of inhibitory interneurones on dLGN cells (Sillito & Kemp, 1983; Montero & Singer, 1984, 1985) and that ionophoretic application of the GABA antagonist bicuculline will block binocular inhibition in the dLGN (Burges, Grieve, Murphy & Sillito, 1985; Pape & Eysel, 1986). Taking note of the fact that layer VI cells in the visual cortex are best activated by moving bars (Gilbert, 1977; Harvey, 1980; Tsumoto & Suda, 1980), we have examined the responses of dLGN cells to a moving bar sweeping over the non-dominant eye field in the presence and absence of inhibitory blockade. We have compared the data obtained both with and without corticofugal feedback in order to assess the contribution of the corticofugal fibres.

METHODS

The experiments were carried out on twenty-two anaesthetized (70% N_2O, 30% O_2, 0·1–0·4% halothane), paralysed (10 mg/(kg h) gallamine triethiodide) female cats in the weight range 2·0–2·5 kg, prepared as described previously (Kemp & Sillito, 1982; Sillito & Kemp, 1983). End-tidal CO_2, the ECG waveform, intersystolic interval and EEG waveform were monitored at all times throughout the experiments. Variations from set levels of these parameters triggered a visual and audio alarm system. Any variations of the parameters commensurate with a decline in the level of anaesthesia were immediately compensated for by an increase in the level of halothane.

Single-unit recordings were made in the A laminae of the dLGN, using multibarrelled glass micropipettes containing Pontamine Sky Blue (2% w/v) in 0·5 M-sodium acetate in the recording barrel, and the following drug solutions; *N*-methyl-bicuculline (NMB, Sigma, 5 mM in 165 mM-NaCl, pH 3·0), γ-aminobutyric acid (GABA, Sigma, 0·5 M, pH 3·0) and either acetylcholine chloride (ACh, Sigma, 0·2 M, pH 4·5) or quisqualic acid (Sigma, 15 mM, pH 8·5).

Cells were mapped and classified as X- or Y-type according to their dominant eye responses. A battery of standard tests was employed (Enroth-Cugell & Robson, 1967; Derrington & Fuchs, 1979). In particular we checked the linearity of spatial summation utilizing sinusoidally reversing sinusoidal gratings presented at a range of spatial phases in a randomized interleaved sequence. We also noted receptive field centre size, the strength of centre–surround inhibition and the presence or absence of a shift effect. The cells were then stimulated through the non-dominant eye alone, at the retinal location corresponding to the dominant eye receptive field, with a moving bar of light. The parameters of this stimulus were varied in the range of 10–22 deg for length, 0·2–1 deg for width and 2–20 deg for velocity. In some cases we explored the effect of varying stimulus orientation.

The basic experimental protocol involved testing the non-dominant eye response to a moving bar under control conditions and then comparing this with the response obtained during ionophoretic application of the GABA antagonist bicuculline. The effectiveness of the GABA blockade was checked by determining the reduction in the inhibitory effect of a 'reference' pulse of ionophoretically applied GABA. This reference was established by determining the ejection current necessary under control conditions to completely suppress the response of the cell to a spot of light flashed within the centre of the dominant eye field. The inhibitory blockade was only considered viable when the 'reference' GABA pulse ceased to affect the dominant eye spot response. The application of bicuculline frequently raises the background discharge level and we controlled for this effect by checking the responses obtained when the resting discharge was raised by ionophoretic application of either acetylcholine or quisqualate, an excitatory amino acid (Kemp & Sillito, 1982). In fact increasing the resting discharge with either of these agents could reveal the presence of a stimulus-driven suppression of unit activity and was routinely used to

check for inhibitory effects in cells with low resting discharge levels. In order to assess the contribution of the corticofugal projection, recordings were made simultaneously from left and right dLGNs, and visual cortical areas 17 and 18 on one side were removed by aspiration. The response to non-dominant eye stimulation were then compared for the cells with and without corticofugal feedback.

Responses were quantified as follows. The apparent width of the receptive field was determined from the peristimulus time histogram. The change in activity of the cell, averaged over the entire response zone, was then calculated and expressed as a percentage of the on-going spontaneous or drug-induced discharge. In addition, the average frequency of excitatory responses was recorded in impulses per second above background level.

Recording sites were marked with Pontamine Sky Blue and identified histologically. Blocks of visual cortex encapsulating the lesioned and damaged areas were immersed in 10% (w/v) formal saline for a period of several weeks, with frequent changes of solution. The tissue was then impregnated with a solution of 1% gum arabic and 30% sucrose to protect against freezing damage, and embedded in a gelatine–albumin block that was fixed by denaturing with glutaraldehyde. Frozen sections (50 μm) were cut in the coronal plane, mounted and stained with Neutral Red. The zone of damage was fully reconstructed by comparison with the intact hemisphere, and the extent of the lesion assessed with respect to the visual field maps of Tusa and colleagues (Tusa, Palmer & Rosenquist, 1978; Tusa, Rosenquist & Palmer, 1979).

RESULTS

Our data are summarized in Fig. 7 and described in detail below. They derive from a total population of seventy-four cells recorded in the A laminae of the dLGN, of which thirty-seven had X- and thirty-three had Y-type fields. All had receptive fields within 12 deg of the area centralis. We have explicitly excluded three binocular cells encountered within the interlaminar zone from this study.

Non-dominant eye responses in the normal dLGN

Out of a population of fifty-seven cells, forty-three (75%, twenty Y, twenty-three X) had a non-dominant eye receptive field in the absence of inhibitory blockade. This was revealed as the light bar passed over a retinal location corresponding to that of the dominant eye field. Responses were small and labile, and were generally seen only by averaging a large number of individual trials (20–100). In most cases (86%, thirty-seven out of forty-three, seventeen Y, twenty X) there was a suppression of the spontaneous or drug-induced discharge, whilst three cells (7%) exhibited both excitatory and inhibitory components to the response, and three (7%) showed a pure excitation. These figures are very similar to those reported by Sanderson and co-workers (1971). In every case tested where a cell had a non-dominant eye input (thirty-two), the ionophoretic application of NMB at currents that produced an effective blockade of the action of exogenously applied GABA, also blocked stimulus-driven inhibition. Furthermore, in 84% of these cells (twenty-seven out of thirty-two) and three cells previously unresponsive to the non-dominant eye, NMB application uncovered a clear excitatory input. A further five cells originally unresponsive to the non-dominant eye remained so during inhibitory blockade. Thus 75% of the cells tested with NMB (thirty out of forty, thirteen Y, seventeen X) exhibited a non-dominant eye excitatory response.

Figure 1 illustrates typical results obtained for an on-centre Y cell recorded in lamina A. The upper record shows the control condition. The on-going background

discharge was depressed as the stimulus passed over the non-dominant eye receptive field, in both directions of motion. The width of the inhibitory field averaged 2·25 deg for the two directions of motion, and over this zone the activity of the cell was reduced by an average of 62·5% with respect to the background discharge. The application of NMB had a twofold effect. The inhibition was blocked, and after 3 min

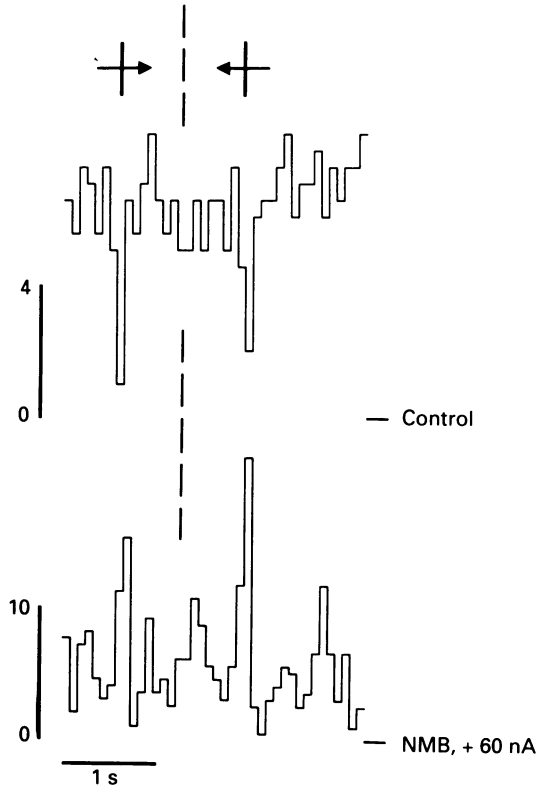

Fig. 1. Effect of inhibitory blockade on the non-dominant eye responses of an on-centre Y cell. Peristimulus time histograms show responses to a bar of light sweeping forward and backward over the receptive field, averaged for twenty-five trials. Upper record is the normal response (control), lower record the response during ionophoretic application of *N*-methyl-bicuculline (NMB). The inhibition elicited under control conditions can be seen to have masked an underlying excitatory input. Vertical calibration refers to response frequency in impulses/s. Bin size, 75 ms. Horizontal calibration shows 1 s time period.

was replaced by an excitatory response from the corresponding portion of the visual field. The unmasked response was clear and involved a 185% increase over background discharge averaged over a 3 deg field. A further example, this time for an on-centre X cell, is given in Fig. 2. Here, under control conditions the width of the suppressive field averaged 3·5 deg for the two directions and the response was reduced by an average of 42%. During inhibitory blockade the original response was replaced by excitatory peaks showing a 64% increase over background. The records document recovery from the effects of the blockade at 6 and 16 min after cessation of drug application. At 6 min there was clearly some excitation to one direction of motion but at 16 min the inhibitory response had returned. It is relevant to note that

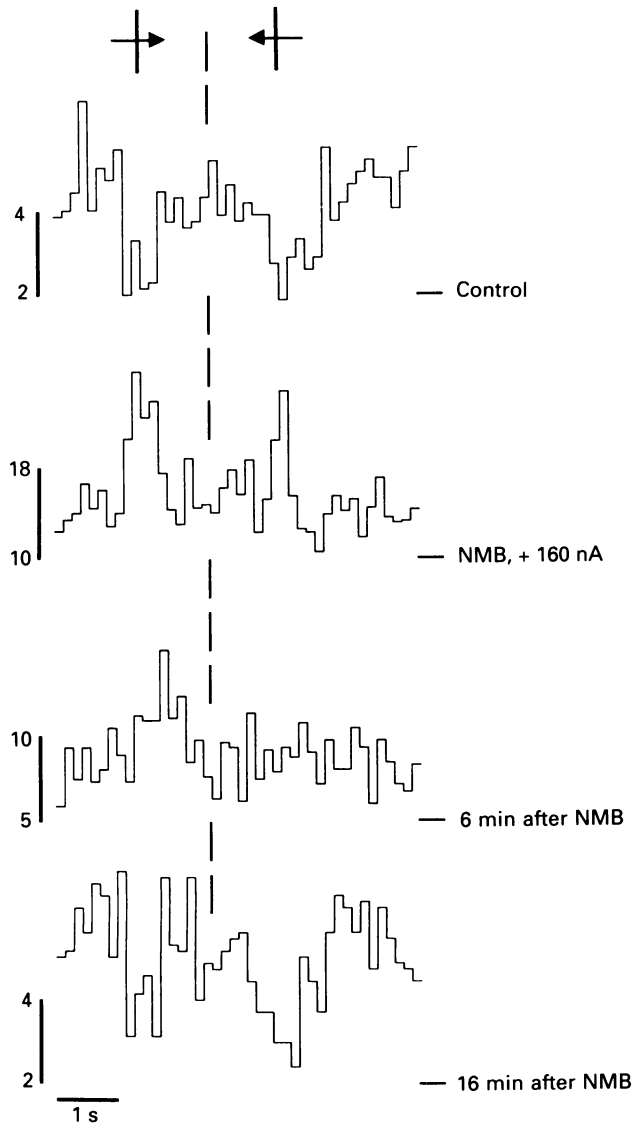

Fig. 2. Responses of an on-centre X cell before, during and after inhibitory blockade. Records averaged over fifty trials. Bin size, 125 ms. Vertical calibrations refer to response frequency in impulses/s. Other details as for Fig. 1.

all the responses described here for the non-dominant eye were substantially weaker than those elicited by stimulation of the dominant eye field. They could only be reliably detected by long periods of averaging.

Finally, excitatory effects were not obtained when resting discharge levels were increased by ionophoretic application of quisqualate or ACh. Indeed, in certain individual cases it enhanced the effectiveness of the inhibition, although it made no significant difference to the population as a whole. These findings are illustrated in Fig. 3, the upper record of which shows the effect of ionophoretic application of ACh, at an ejection current of +1 nA, on the non-dominant eye response of the cell shown

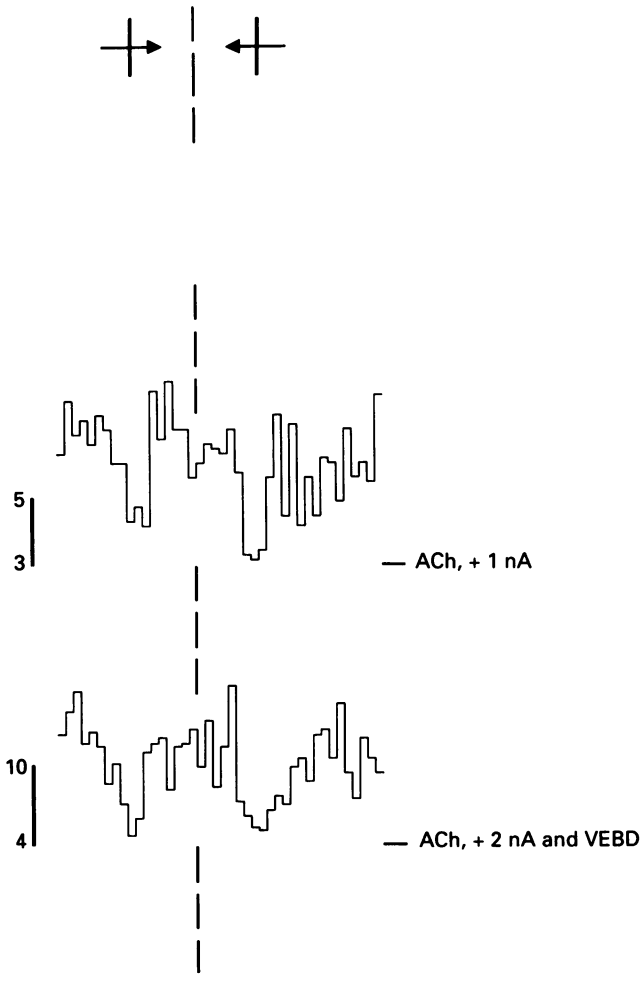

Fig. 3. Effect of altering background discharge level on the non-dominant eye responses of the cell in Fig. 2. Upper record, effect of ionophoretic application of acetylcholine at a low current to slightly elevate background discharge on visual response. Lower record, effect of elevation of background discharge by visual stimulation of the dominant eye field (VEBD) and ionophoretic application of ACh. This combination raised the discharge level of this cell to the same extent as NMB (Fig. 2) but did not modify the non-dominant eye inhibitory response. Vertical calibrations, impulses/s.

in Fig. 2. The drug almost doubled the background discharge of the cell. The lower record shows the result of raising the background discharge still further, to the same level as that induced by bicuculline application, by combining ACh excitation with visual driving from the dominant eye. In neither case was the inhibitory response significantly decreased from control levels.

Effects of removing the corticofugal input

We recorded from fourteen A laminae cells of geniculate nuclei deprived of feedback from areas 17 and 18 of the visual cortex, and compared their responses to non-dominant eye stimulation directly with those of cells recorded in the control dLGN of the same animal, and with the pooled results described above. The primary

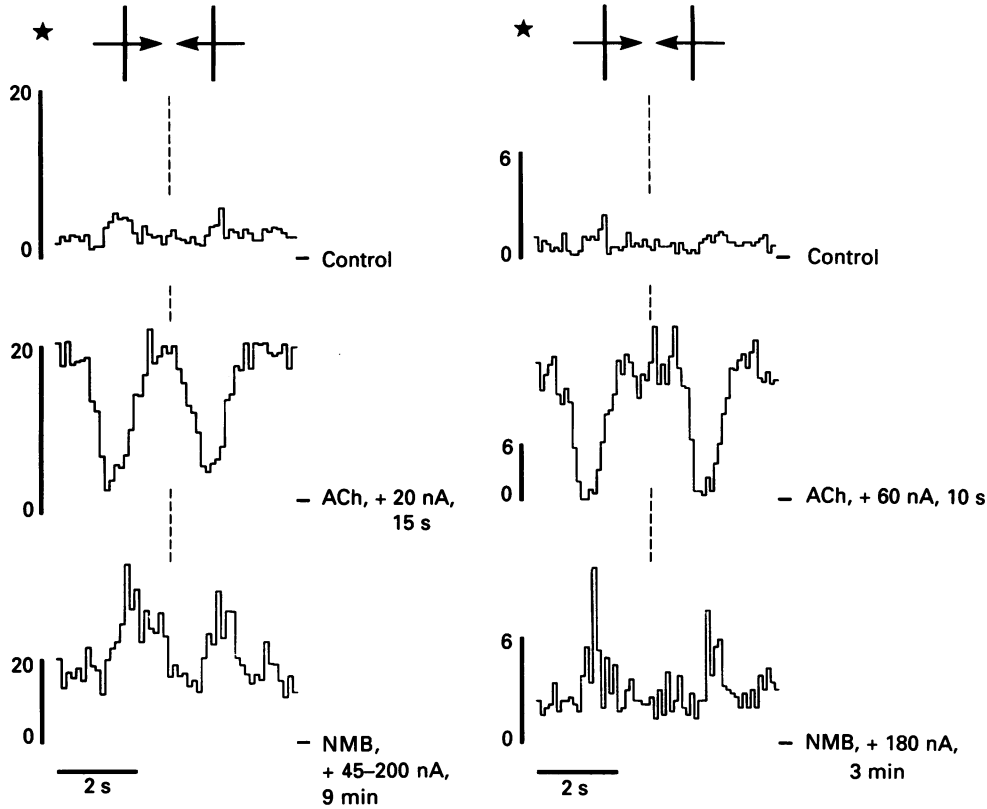

Fig. 4. Non-dominant eye responses in the absence of corticofugal feedback. Records in left and right columns show respectively the responses of an off- and an on-centre Y cell. Responses are documented under control conditions (upper records) and in the presence of ionophoretically applied acetylcholine (middle records) and NMB (lower records). Responses averaged over fifty trials; bin, size, 100 ms; vertical calibrations, impulses/s. Both cells gave a small excitatory response under normal circumstances and this was greatly increased by NMB. In contrast, raising the background discharge of the cells with ACh elicited a powerful visually driven inhibition.

finding was the surprising observation that in every case, non-dominant eye inhibition and excitation survived removal of the corticofugal influence. This is illustrated in Fig. 4.

An example of the extent of the cortical ablations is given in Fig. 5, which refers to the preparation from which the off-centre Y cell in Fig. 4 was recorded. There is no doubt that this lesion would have removed the corticofugal input to the A laminae of the dLGN at the visual field eccentricities covered in this study. These lesions were

not without effect, however, since the pattern of response in the decorticate dLGN differed somewhat from that seen in the control population.

The first distinction between the normal cells and those that were deprived of corticofugal feedback was in the ease with which a non-dominant eye receptive field could be demonstrated. The cells on average responded more clearly than those in the normal preparation, and in every case a response was immediately obvious for the first combination of stimulus parameters tested. Furthermore, in marked contrast to

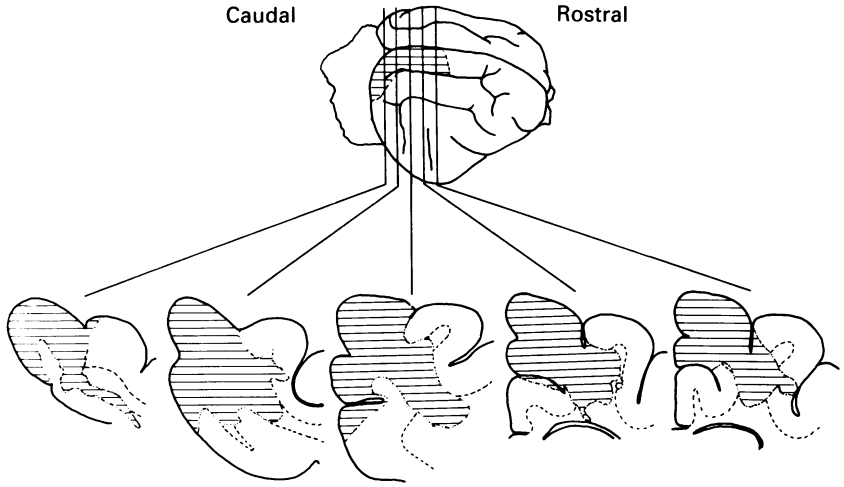

Fig. 5. Histological reconstruction of the area of removal of areas 17 and 18 of the right-hand-side visual cortex associated with the data for the off-centre Y cell in Fig. 4. Cross-hatching represents areas of total tissue ablation, with respect to the surface view (top) and a series of representative coronal sections.

the proportion recorded under normal conditions, only 46% (six out of thirteen, two Y, four X cells) of the control responses were purely inhibitory. The remaining cells all had a clear excitatory response, in three cases mixed with varying degrees of inhibition. Hence there was an increase in the prevalence of excitatory responses prior to inhibitory blockade. For example, the upper records in Fig. 4 illustrate the control results for an off-centre Y cell of layer A and an on-centre Y cell of layer A1, following lesion of the corticofugal pathway. Both responded with an excitatory discharge which, although small, doubled the firing frequency of the cells in the first direction of motion of the stimulus. In contrast, the cell illustrated in Fig. 6, an off-centre X cell, had a broad inhibitory field enclosing clear facilitatory peaks. This latter was classified as a mixed response, since it was presumed to be generated by the excitatory input also received by this unit.

The application of either ACh or quisqualate shifted the balance described above in a dramatic fashion. In every case, raising the background activity of the cells in this way revealed a profound and extensive suppression of the driven discharge as the stimulus passed over the non-dominant eye receptive field. This shift is evident for the two cells illustrated in Fig. 4 (middle records), both of which had an inhibitory field 7 deg in width, generating a suppression of 54% and 61% respectively when averaged over the entire field. An inhibition of this extent and magnitude was not

seen in the normal dLGN, either in the control condition or in conditions of raised excitability, yet was entirely typical of the results obtained following cortical ablation.

The effects of bicuculline were tested on eleven cells (seven Y, four X). Inhibitory blockade revealed excitatory responses in all those previously showing only suppression of their activity and enhanced the excitations initially exhibited by the others. These effects were observed in most cases within 1–3 min of drug onset. For

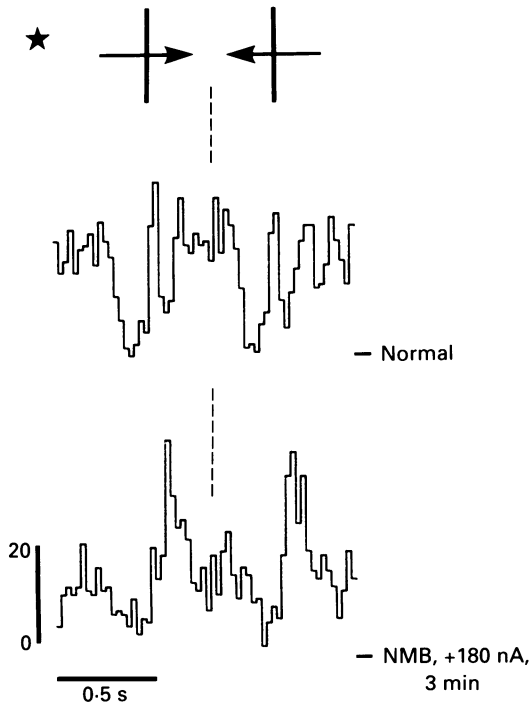

Fig. 6. Response of an off-centre X cell in the absence of corticofugal feedback, before and during inhibitory blockade. Average of fifty trials. An excitatory input to this cell was evident even in the control condition, when it sat within a broader pool of inhibition. Blocking this inhibition with NMB revealed the excitation more clearly. Bin size, 25 ms; vertical calibration, impulses/s.

the population as a whole, the final signal-to-noise levels of the non-dominant eye responses were substantially greater than those recorded in the normal dLGN, even though the responses used in the analysis were measured on average after a far shorter period of drug application. Hence the excitation elicited through the non-dominant eye appeared to be more prominent and easily revealed in the absence of corticofugal feedback than in the normal situation. For example, after only 3 min under the influence of NMB, the cells illustrated in Fig. 4 had a response frequency of respectively 93 and 103% greater than background, for fields averaging 5·5 and 3·25 deg in width. An equally rapid onset and clear excitatory response was seen even in those cells which initially showed strong inhibition, such as that illustrated in Fig. 6, where the excitation after 3 min had increased to 93% above background for a 3·5 deg

field width. However, it should be stressed that these data do not necessarily imply that the magnitude of the input is increased by removal of the corticofugal feedback. It was found that the background discharge of the cells in the cortex-deprived dLGN was significantly lower on average during NMB application than in the normal preparation (6 ± 2 impulses/s compared with 20 ± 3 impulses/s), possibly

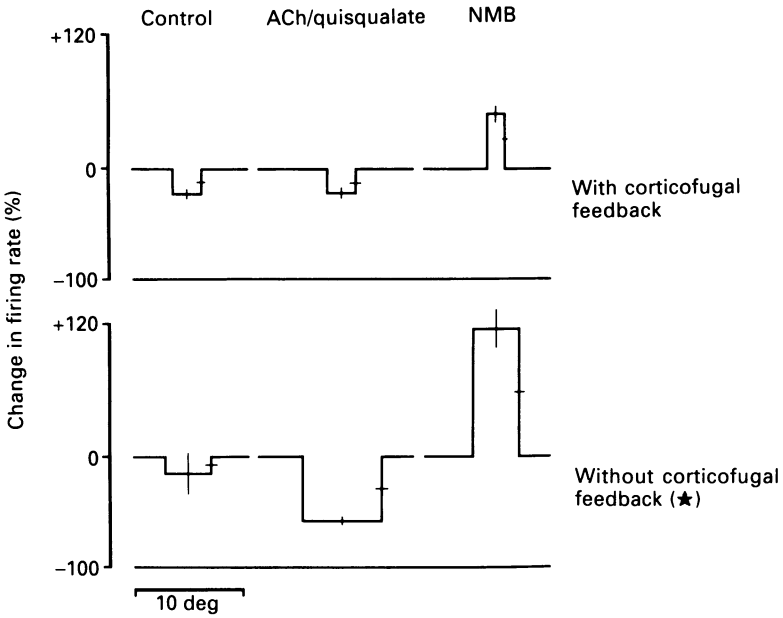

Fig. 7. Diagram summarizing the non-dominant eye responses seen with and without corticofugal feedback, under control conditions and during ACh/quisqualate and NMB application. Response width and percentage change with respect to the background discharge level were calculated for each condition, by averaging the data obtained from all the tested cells (including those with no demonstrable field and those with mixed responses). These figures were then used to construct composite response profiles, with error bars representing standard errors of the mean.

due to the shorter period of drug application. This will necessarily affect the signal-to-noise ratio, and so the absolute frequency of the excitatory response above this discharge level was also calculated. It was found that although the fields tended to be broader, the frequency of response was not significantly different for the two conditions.

Comparison of effects

It is notable that whilst 75% of the cells with corticofugal feedback exhibited a non-dominant eye response prior to inhibitory blockade, 100% of those without corticofugal feedback showed a response with 50% of these, as opposed to 10%, exhibiting excitation. Similarly during inhibitory blockade 100% of the cells lacking feedback exhibited excitatory responses as opposed to 75% of the normal cells. Figure 7 compresses these data into a set of composite non-dominant eye responses relating to the six stimulation conditions. These were generated by averaging the

results of all the cells tested, including 'no effects' and mixed responses, for each condition and drawing the resultant response with respect to an arbitrary background activity level. This highlights the more notable effects of the cortical lesion: the shift in the apparent gain of the inhibitory input under conditions of raised excitability, seen only in the cells without feedback, and the increase in the signal-to-noise level of the excitatory input following GABA blockade.

Non-dominant eye receptive field properties

This work obviously raises questions regarding the nature of the receptive field properties of the excitatory inputs revealed in the non-dominant eye. In fact, given the long averaging procedures necessary to resolve responses, it proved virtually impossible to obtain a satisfactory quantitative evaluation of receptive field properties within the feasible duration of a period of continuous NMB application. However we did ascertain that the cells would sometimes give small 'on–off' responses to spots of light flashed in the discharge zone defined by the moving bar. There was no obvious centre–surround organization and the responses were not orientation tuned. It did appear that a long moving bar, as utilized in these experiments, was the most effective way of demonstrating the non-dominant eye responses and would reveal changes where a stationary flashing spot exerted no obvious effect.

DISCUSSION

Our data provide clear evidence that the majority of both X and Y cells in the A laminae of the dLGN receive an excitatory as well as an inhibitory input driven by the non-dominant eye. The ability of ionophoretically applied bicuculline to block the non-dominant eye-elicited inhibition and reveal excitatory responses is commensurate with previous observations (Burges *et al.* 1985) and argues strongly in favour of the role of GABA as the transmitter mediating this input. This is consistent with evidence supporting the role of GABA in other inhibitory processes within the dLGN (Sillito & Kemp, 1983). Our failure to demonstrate excitatory responses in a small number of cases could well reflect a limited effectiveness of the blockade of inhibitory synapses (as opposed to the pharmacological blockade of ionophoretic GABA) rather than the absence of the relevant inputs. The inhibitory synapses are distributed over the dendrites of the relay cells (Wilson *et al.* 1984) and the positioning of the electrode with respect to the cell could well be critical for an effective drug distribution, particularly with respect to those synapses that are at more remote locations. An alternative possibility is that there is a variable level of contribution from $GABA_B$ receptors, which would be unaffected by bicuculline application. From this viewpoint it would be interesting to examine the effects of the $GABA_B$ antagonist phaclofen. However this query only refers to five out of thirty-five cells for which an inhibitory field was identified and an effective pharmacological blockade of ionophoretically applied GABA achieved. The major point is that we have shown that a much larger proportion of cells receive a non-dominant eye excitatory input than previous studies have suggested (Sanderson *et al.* 1971).

The number of cells actually receiving non-dominant eye excitation is entirely

consistent with what might be predicted from present knowledge regarding the corticofugal projection to the dLGN. It is thus somewhat paradoxical that we should find that the excitatory effects survive removal of the corticofugal input. In anatomical terms at least, the input from the visual cortex to the dLGN is massive, providing between 40 and 50% of the excitatory contacts to A laminae relay cells (Wilson *et al.* 1984). Although the synapses tend to occur on distal dendrites and might therefore be presumed to exert a weaker influence, the electrotonic properties of the dLGN cell dendrites appear to be such that the distal and proximal synaptic inputs can be regarded as equivalent (Bloomfield, Hamos & Sherman, 1987). Our visual stimuli were ideally suited for activating this input, which arises in part from binocular cells (Gilbert, 1977; Harvey, 1980; Tsumoto & Suda, 1980) and in addition innervates the dLGN in a non-layer-specific manner (Updyke, 1975; Robson, 1983; Boyapati & Henry, 1984). Even allowing for the presence of an alternative source of binocular input, one would expect that the removal of the cortex should substantially reduce the magnitude of the non-dominant eye excitation. Since this was not the case, it seems necessary to postulate that the corticofugal input also generates an inhibitory influence that 'balances' the cortical contribution to the non-dominant eye excitation, and that a significant component of this is resistant to our inhibitory blockade. It is clear that this input innervates inhibitory neurones of both the perigeniculate nucleus (PGN) and the dLGN itself (Updyke, 1975; Ide, 1982; Robson, 1983; Montero & Singer, 1984, 1985) and hence can potentially provide a strong inhibitory drive. Indeed, evidence for such a corticofugally mediated inhibition has been given elsewhere (Murphy & Sillito, 1987). From this viewpoint it is interesting to note the shift in the balance of inhibitory and excitatory non-dominant eye effects, observed following removal of the cortical input. In the absence of corticofugal feedback, an excitatory drive was initially evident in a larger percentage of cells, and was very rapidly unmasked by the application of bicuculline in all other cases. This is consistent with a reduction in the level of the non-dominant eye inhibitory inputs following the removal of the cortical excitatory drive to geniculate and perigeniculate GABAergic interneurones, and can be interpreted as further evidence of an inhibitory bias in the corticofugal pathway.

The consequences of removal of the corticofugal input, however, cannot be simply attributed to a reduction in the effectiveness of the inhibitory drive in the dLGN. From another viewpoint our data suggest exactly the converse. In the absence of corticofugal feedback, raising the background discharge of a dLGN cell with ACh or quisqualate resulted in the replacement of the excitatory response with a very potent, visually driven inhibition of the activity. Accepting that ACh hyperpolarizes intrinsic inhibitory interneurones in the dLGN (McCormick & Pape, 1988), this effect is unlikely to follow from a direct action of the drug on adjacent inhibitory interneurones. The most likely explanation is that the increased resting discharge level of the relay cells enhanced the level of excitability of perigeniculate inhibitory interneurones via the excitatory collateral input to this nucleus, hence increasing the inhibitory feedback from the perigeniculate nucleus. Following from this, the data suggest (Fig. 7) that the strength and duration of both the inhibition observed during periods of artificially raised excitability, and of the excitation observed during bicuculline application, were significantly greater than those seen in the

normal preparation. Removing the corticofugal feedback therefore appeared to increase rather than decrease the expression of both excitatory and inhibitory inputs, under suitable conditions. This suggests that under our experimental conditions the corticofugal input acts in a way which minimizes the modulation of neuronal firing consequent upon the non-dominant eye input. This might follow from a simple phase shift in the corticofugal excitatory and inhibitory modulation with respect to that from subcortical structures.

These data raise the further question of the source of the non-dominant eye excitation. The vast majority, if not all, of the cortico-thalamic pathways to these cells arises in areas 17 and 18. Area 19 feeds back to the C laminae, as does a component of the pathway from the posterior medial lateral suprasylvian area (PMLS) (Kawamura, Sprague & Niimi, 1974; Updyke, 1981), but neither appear to project to the A laminae. Indeed the only other extrageniculate source of visual input to the A laminae comes from the nucleus of the optic tract (Graybiel & Berson, 1980), and this must be considered a potential source of the excitatory drive reported here. The remaining alternative is an input at geniculate level. The retinal afferents appear to be well segregated (Hickey & Guillery, 1974; Sur & Sherman, 1982; Bowling & Michael, 1984), so any direct innervation would have to contact relay cell dendrites that cross from one lamina into the next. Distal dendrites, especially of Y cells, are known to do this and so the explanation is possible on anatomical grounds (Friedlander, Lin, Stanford & Sherman, 1981). It has been claimed that retinal inputs are largely confined to the proximal dendrites of relay cells (Wilson *et al.* 1984; Robson, 1983), but this rule is not absolute (Hamos, van Horn, Raczkowski & Sherman, 1987) and no-one has specifically investigated dendrites that pass out of the layer of origin. Furthermore, the compact electrotonic properties of both X and Y cells could well permit an effective level of driving from even a small number of distally located synapses, in the absence of normal inhibitory control (Bloomfield *et al.* 1987). Another possibility is that the excitation originates from collaterals of the relay cells themselves.

The presence of subcortical binocular facilitatory and inhibitory inputs to dLGN relay cells provokes two suggestions. One is that because they are weak, they essentially reflect the contribution from 'aberrant' connections and the corticofugal pathway serves to minimize the impact of these on cortical binocular function. This is consistent with our finding that they appear to be suppressed or 'balanced out' in the intact preparation, during monocular stimulation. Alternatively, taking note of the strength of the corticofugal projection, and its obvious potential for binocular influence, it is tempting to suggest that they subserve a specific role as yet undefined in the generation of binocular vision. There certainly is a precedent for this latter view (Schmeilau & Singer, 1977; Varela & Singer, 1987; Xue, Ramoa, Carney & Freeman, 1987). For the dominant eye responses we have recently shown that the corticofugal pathway exerts a potent control over the specificity for stimulus length and position of the receptive field (Murphy & Sillito, 1987). A similar role in dLGN cell responses to binocular stimuli must be considered plausible.

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