Modification of Orientation Sensitivity of Cat Visual Cortex Neurons by Removal of GABA-Mediated Inhibition

T. Tsumoto, W. Eckart, and O.D. Creutzfeldt

Department of Neurobiology, Max-Planck-Institute for Biophysical Chemistry, Postfach 968, D - 3400 Göttingen-Nikolausberg, Federal Republic of Germany

Summary. The effects of an inhibitor of GABA synthesis, 3-mercaptopropionic acid (MP), and of the GABA antagonist bicuculline (BIC), on the direction and orientation sensitivity of visual cortical neurons were investigated using a computer-controlled stimulus presentation system. Intravenous administration of MP, which was usually more effective than if administered microelectrophoretically, induced a slight, but significant reduction in these properties of about half of the neurons tested. The effect of electrophoretic BIC was in the same direction but clearer than that of MP. In 71% of the simple cells, direction sensitivity was virtually lost during administration of BIC while orientation sensitivity was never completely eliminated in any neuron tested. Simultaneous administration of both drugs (MP systemically, BIC electrophoretically) caused more complete modification of the sensitivities than single administration of each. In four out of thirteen neurons tested, orientation sensitivity was completely abolished. The excitatory receptive fields slightly increased in size and became virtually round. The response magnitude to the optimal stimulus was increased by each drug alone and by both. The present results further support the hypothesis that intracortical inhibition plays a major if not an exclusive role for the orientation and direction sensitivity of cortical cells.

Key words: Visual cortex – Orientation sensitivity – GABA-inhibition – Bicuculline – 3-Mercaptopropionic acid.

Visual cortical (VC) neurons are preferentially or selectively responsive to particular visual stimulus parameters, such as to the orientation of a light slit or dark bar of a specific orientation moving in one direction (Hubel and Wiesel, 1962). Several lines of evidence suggest that the orientation and direction...
sensitivity may be partially due to intracortical inhibitory mechanisms (Creutzfeldt and Ito, 1968; Benevento et al., 1972; Blakemore and Tobin, 1972; Bishop et al., 1973; Creutzfeldt et al., 1974). If this is so, pharmacological blockade of intracortical inhibition should be able to abolish or attenuate those sensitivities of VC neurons.

There is abundant evidence suggesting that gamma-aminobutyric acid (GABA) may be an inhibitory transmitter in VC (Mitchell and Srinivasan, 1969; Iversen et al., 1971) and that its action is selectively antagonized by the alkaloid biccuculline at postsynaptic sites (Curtis et al., 1970, 1971; Curtis and Johnston, 1974; Sillito, 1975a). Using intravenous biccuculline, Pettigrew and Daniels (1973) reported that VC neurons of the complex type lost some of their sensitivities but simple cells did not. In both types of cells, Rose and Blakemore (1974) found that topical application of the same drug reduced such sensitivities and increased the size of their excitatory receptive fields (RF). More recently, Sillito (1975a, b, 1977) reported that in simple cells the direction sensitivity was significantly reduced or eliminated but the orientation sensitivity was only slightly reduced, whereas in complex cells the latter was virtually lost. Although the results of these three groups are not fully consistent with each other, each supports only partially the hypothesis described above. This may be due to an incomplete block of inhibition, because the GABA-induced or electrically elicited inhibition of some cortical neurons was not blocked by biccuculline (Curtis and Felix, 1971; Sillito, 1975a).

In the present experiments an inhibitor of GABA-synthesis, 3-mercaptpropionic acid (MP), was used in an attempt to abolish GABA-inhibition. MP was reported to produce convulsions in mice (Sprinze et al., 1969), and to markedly reduce the concentration of GABA in the cerebral or cerebellar cortex (Rodríguez de Lores Arnaiz et al., 1972, 1973; Karlsson et al., 1974). This effect of MP is suggested to be due to inhibition of glutamate decarboxylase which is directly involved in GABA synthesis (Lamar, 1970; Rodríguez de Lores Arnaiz et al., 1972, 1973; Karlsson et al., 1974; Wu, 1975). In a third step of our experiments, MP and biccuculline, which may thus act separately on pre- and postsynaptic sites, were administered simultaneously.

Methods

Preparation

The experiments were done on fourteen adult cats. Under sodium pentobarbitone (Nembutal) anaesthesia (i.p., 30–40 mg/kg), the trachea and femoral vein were cannulated for artificial ventilation and infusion, respectively. The animals were immobilized by an i.v. infusion of gallamine triethiodide (9–12 mg/kg/h). Since the experiments mostly took up to 48 h, 20–30 mg Nembutal was added every 6–8 h. Further details of the preparation and care of the animals throughout the experiments are given elsewhere (Tsumoto et al., 1978).

Administration of Drugs

Four-barrel micropipettes, consisting of two double-chambered pipettes (theta-pipettes) were used for the extracellular recording of neuron activity and the electrophoretic administration of drugs.
One channel of a recording theta-pipette was filled with a solution of 2-M NaCl and the other with 1-M NaCl solution saturated with Fastgreen dye for histological identification of the recording site. A second theta-pipette was attached to the recording pipette which protruded 20–30 µm beyond the orifice of the former pipettes (Hess and Murata, 1974; Tsunomo et al., 1978). In most of the experiments, both channels of the second pipettes contained a solution of bicuculline (5 mM in 165 mM-NaCl, adjusted to pH 3 with HCl) or a solution of MP (2 mM in 165 mM-NaCl, adjusted to pH 6 with NaOH). In some experiments, one channel was filled with the bicuculline and the other with the MP solution. The ejecting currents for bicuculline and MP were +20 to +150 and −50 to −200 nA, respectively. To prevent leakage of the drugs from the micropipette tips, the retaining currents of −20 and +30 nA were passed through the pipettes with bicuculline and MP, respectively. In most of the experiments, MP was administered intravenously via the cannulated femoral vein with an infusion pump. For this, a solution of 2% MP in 165 mM NaCl was infused at a rate of 15–20 mg/kg/h. The EEG was recorded continuously from the sensorimotor cortex ipsilateral to the recording site. When convulsive signs were observed in the EEG, administration of MP was stopped.

**Recordings and Visual Stimulation**

Penetrations were made through a closed chamber overlying area 17 of the cortex. Amplification and display techniques for unit activity were conventional. After a unit was isolated, its excitatory RF was plotted with hand-held black or bright targets. For quantitative analysis of orientation and direction sensitivities, a moving light slit or dark bar was projected from the rear onto a screen located 1 m in front of the cat. Movement, orientation, and direction of the bar were computer controlled by moving a mirror system in the path of the projection beam. Orientation and movement direction were changed after each sweep and the response stored. Peristimulus time histograms (PSTHs) for the forward and backward movements at each orientation were constructed after completion of the desired number of stimulus cycles. The rotation started from the optimal orientation in a clockwise fashion at steps of 30 or 45° so that forward and backward movements at different orientations were tested in each unit. In the following section (results) the different orientations are represented as the optimal, the clockwise (+) or anticlockwise (−) deviations at 30 or 45° intervals and at the orientation 90° from the optimal.

PSTHs at each orientation were constructed from 3–8 sweeps with a bin width of 5–40 ms. Starting and returning points of the stimulus at each orientation were arranged so that the stimulus always crossed the center of the excitatory RF of the recorded cell. After a complete set of PSTHs had been calculated, the computer could display all the PSTHs simultaneously, or an enlarged PSTH at a given orientation alone. Also, it could display a polar plot or orientation tuning curve based on the amplitude of the averaged responses. Usually, the stimulus was 1.0–1.5 log units above or below the background illumination, which was kept in the scotopic–mesopic range (about 10⁻⁵ cd/m²). Only one eye was stimulated. In order to assess drug effects, the same stimuli were given and PSTHs were constructed before, during and after administration of the drugs.

**Results**

The present report is based on 60 neurons recorded from area 17 of the cortex. Twenty-five of them were studied with MP, 20 with bicuculline and 15 with both drugs.

**Effects of MP**

In preliminary experiments MP was administered intraperitoneally (25–30 mg/kg) after having identified the RF-properties of a unit and constructed a set
<table>
<thead>
<tr>
<th>Opt</th>
<th>+30°</th>
<th>+60°</th>
<th>+90°</th>
<th>-60°</th>
<th>-30°</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Fig. 1.** Effect of MP on orientation and direction sensitivity of a complex cell. Direction of motion and orientation of the slit (0.5° × 6°) are indicated by diagrams above each PSTH in A. Relative values of the orientation to the optimal are given in the left of A. Stimulus speed was about 6º/s. Four sweeps for each PSTH, bin width 7 ms. Vertical calibrations at the foot of A indicate 16 spikes/bin. A control PSTH-set made before MP administration. B PSTH-set obtained during intravenous infusion of MP. Records were taken 28–32 min after starting the infusion. C control PSTH-set made 62–66 min after stopping the infusion.

of control PSTHs. About 10 min after i.p. injection, the EEG showed very large slow waves and sharp seizure potentials, eventually leading into status epilepticus. Simultaneously, the cells discharged in high frequency clusters, independent of visual stimuli and then became silent, probably due to depolarization block. After some 10 min, the EEG recovered to the original state, but the unit was usually lost. When a smaller dose was given, the EEG, cell activities and responses were not significantly altered. These observations indicate that the tolerance range for the action of MP is very narrow, and that intraperitoneal administration was not suitable for our experiments.

As described later, electrophoretic MP exerted weaker effects on the stimulus selectivity of VC neurons than intravenous MP. In most experiments, therefore, MP was administered intravenously (see methods). An example of
Table 1.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Type of units</th>
<th>No. of units</th>
<th>Orientation sensitivity</th>
<th>Direction sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>reduced&lt;sup&gt;a&lt;/sup&gt;</td>
<td>abolished&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>MP</td>
<td>simple</td>
<td>9</td>
<td>3 (33%)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>complex</td>
<td>10</td>
<td>6 (60%)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>unclas.</td>
<td>6</td>
<td>2 (33%)</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>25</td>
<td>11 (44%)</td>
<td>0</td>
</tr>
<tr>
<td>Bic.</td>
<td>simple</td>
<td>8</td>
<td>2 (25%)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>complex</td>
<td>7</td>
<td>5 (71%)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>unclas.</td>
<td>5</td>
<td>2 (40%)</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>20</td>
<td>9 (45%)</td>
<td>0</td>
</tr>
<tr>
<td>MP+</td>
<td>simple</td>
<td>7</td>
<td>4 (57%)</td>
<td>2 (29%)</td>
</tr>
<tr>
<td>Bic.</td>
<td>complex</td>
<td>6</td>
<td>3 (50%)</td>
<td>2 (33%)</td>
</tr>
<tr>
<td></td>
<td>unclas.</td>
<td>2</td>
<td>1 (50%)</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>15</td>
<td>12 (80%)</td>
<td>2</td>
</tr>
</tbody>
</table>

<sup>a</sup> Reduction and abolition of orientation sensitivity during application of the drugs: responses (spike numbers) to motion in the preferred direction of the slit oriented 90° to the optimal increased to 10–49% or to > 50% of those to the optimal stimulus, respectively

<sup>b</sup> Direction sensitivity: the responses to non-preferred and preferred motion direction of the optimally oriented slit were compared

the effect of i.v. MP on the responses of a VC neuron is shown in Fig. 1. This neuron was a “complex” cell according to the criteria of Hubel and Wiesel (1962) and had a large excitatory RF (Creutzfeldt et al., 1974). It responded maximally to a slit moving from the left to the right at the optimal orientation (−30° to the vertical) and had a wide response field (top of A). Significant responses were also elicited by the moving slit if the orientation deviated ±30° from the optimal. Thus, the “orientation tuning” of this unit was broad, as is usual for complex cells. Thirty minutes after starting the continuous i.v. infusion of MP, the responses to the preferred motion of the slit at optimal and ±30° orientations were markedly increased (B). Slight responses were also elicited by all other orientations. Thus, MP produced a slight, but significant reduction of the direction and orientation sensitivity of this unit. About 60 min after stopping the MP infusion, its responsiveness recovered to the control level (C). Such a reduction of orientation sensitivity by MP was seen in 11 of 25 units tested, and of direction sensitivity in ten of twenty-one direction-sensitive units (Table 1). A cell with RF of unequivocal “hypercomplex” type (Hubel and Wiesel, 1965) was not recorded, and our numbers are too small to suggest differential effects on complex and simple cells. In a few experiments, MP was administered electrophoretically. Fifteen to 30 min after starting the ejection of MP, an increase in the spontaneous discharge and optimal response and a very slight reduction of those sensitivities were observed in some VC neurons.
Fig. 2. Effect of bicuculline on orientation and direction sensitivity of a complex cell. Dashed line in each PSTH shows the turning point of forward and backward movement of a slit (0.5° × 6°). Relative values of orientation of the slit to the optimal are indicated to the left of each PSTH. Stimulus speed was about 5°/s. Four sweeps for each PSTH, bin width 30 ms. The lowest records of A–C are PSTHs of the spontaneous discharge constructed under conditions identical for PSTH compilation in the absence of visual stimulation. Vertical calibration at the foot of A indicates 16 spikes/bin. A control set of PSTHs made before bicuculline administration. B set of time histograms obtained during electrophoretic administration of bicuculline (+ 60 nA). Records were taken 10–14 min after starting the administration. C control set of PSTHs made 20–24 min after stopping the administration.

Effects of Bicuculline

In most VC neurons, electrophoretic bicuculline caused a clearer modification of their specificities than MP. The strongest bicuculline effects observed in our experiments are shown in the example of Fig. 2. This unit was a complex cell, and responded best to forward movements of the slit oriented 40° to the vertical (top of A). The number of spikes elicited by the backward movement of the slit...
was about 40% of that of the optimal response. During administration of bicuculline (+60 nA), responses to the non-preferred motion of the optimally oriented slit increased to the same magnitude as those to the preferred motion (top of B). Thus, the direction sensitivity of this unit was completely eliminated by bicuculline. This confirms previous reports (Pettigrew and Daniels, 1973; Rose and Blakemore, 1974; Sillito, 1975b, 1977; Ostendorf and Hess, 1975; Hess et al., 1976). On the other hand, the orientation sensitivity was not completely abolished, although during bicuculline administration, clear responses could be elicited by slits oriented at ±45° and 90° to the optimal (B). The number of spikes elicited by the slit at 90° to the optimal was 20% of that of the maximal response. In five of seven complex cells the orientation tuning of visual responses was significantly broadened by bicuculline (Table 1), but the responses to the stimulus at 90° to the optimal never exceeded 50% of that to the optimal. The number of simple cells, in which the orientation sensitivity was modified by bicuculline, was relatively small (2 out of 8 cells) and in no case was it abolished (Table 1) (see also Sillito, 1975b; Ostendorf and Hess, 1975; Hess et al., 1976).

Simultaneous Administration of MP and Bicuculline

Since the two drugs appear to act separately on pre- and post-synaptic sites, it was expected that a combination of both might have a stronger effect on orientation and direction sensitivity due to a more complete block of intracortical inhibition than by either drug alone. This turned out to be the case. An example of this is shown in Fig. 3. This neuron was classified as simple. It showed clearly direction-selective responses to motion of the slit at the optimal orientation (A). Orientation tuning of its responses was very sharp, as seen in most simple cells. During the electrophoretic administration of bicuculline (B) the response to the preferred direction was increased and strong responses appeared also in the non-preferred direction (68% of the amplitude to the optimal direction). On the other hand, motion of the slit oriented 90° to the optimal elicited no responses even during bicuculline administration. After the responsiveness had recovered to the original control level (C), MP was infused intravenously. About 20 min after beginning the infusion at the rate of 20 mg/kg/h (D), responses to slit motion in the non-preferred direction at the optimal orientation increased to 48% of those to the opposite motion, but also in this condition, no responses were elicited by the moving slit oriented 90° to the optimal. Bicuculline was then ejected electrophoretically while continuing the intravenous infusion of MP (E). Responses to both directions of motion of the optimally oriented slit increased to 310% of the control response, and also the orientation sensitivity was almost completely abolished. Response magnitudes to forward and backward motion of the slit oriented 90° to the optimal were 84 and 66% of those of the optimal response, respectively. Spontaneous discharges were only slightly increased to a level of 1.1 spikes/sec (see Fig. 4A). Responsiveness of this unit had recovered to the control level about 40 min after ceasing the administration of the two drugs (F). The effects
GABA-Inh

of the sigmoid cell, the effect is oriented.

These graphs illustrate the cells to the loss of the stimulus was to the optical possibility of a saturation.

In two two drugs, abolish the orientation seen that the alkaloid (Fig. 3E) arr

Discussion

The present 3-mercaptopropionic acid reduction of specificity suggests the GABA-mediated that in some electrophorase blocked by the alkaloid MP, on orientation.

Fig. 3. A–F. 1 direction sensitive orientation and of the stimulus vertical calibra administration. Records were ta

Records were ta

administered o addition to cont

min after stopp
of the simultaneous administration of both drugs were not simply summation of the effects of each alone, since each drug had no effects on responses to the slit oriented 90° to the optimal.

These combined drug effects on visual responses of two simple cells are graphically illustrated in Fig. 4. The curves show the magnitude of response of the cells to the eight standard testing stimuli (see methods). In addition to the loss of the direction and orientation sensitivities, the responses to the optimal stimulus were also increased by the drugs, indicating that the control responses to the optimal stimuli without drugs were not "maximal". This excludes the possibility that the loss of orientation and direction sensitivities might be due to a saturation of responses to the optimal stimulus.

In two out of seven simple and two out of six complex cells tested with the two drugs, the combined administration strengthened the effect of each so as to abolish the orientation sensitivity (Table 1). In the cells which lost their orientation sensitivity during simultaneous administration of both drugs, it was seen that their excitatory response fields only very slightly increased in size (see Fig. 3E) and appeared to be virtually round.

Discussion

The present results have demonstrated that simultaneous administration of 3-mercaptopropionic acid (MP) and bicuculline could lead to a remarkable reduction or even complete loss of orientation and direction dependent response specificities of VC neurons, while each drug alone had less clear effects. This suggests that electrophoretic bicuculline may not completely block GABA-mediated inhibition of VC neurons. In fact, previous reports indicate that in some cortical neurons the inhibition, which was induced by electrophoretic GABA or elicited by electrical stimulation, was not totally blocked by bicuculline (Curtis and Felix, 1971; Sillito, 1975a), probably because the alkaloid did not gain access to all of the receptors activated by GABA.

MP, on the other hand, had only weak effects on the direction and orientation specificities of VC neurons if infused intravenously or administered electrophoretically. This may be explained by too low a dose of MP; as long as it

---

Fig. 3. A-F. Effect of simultaneous administration of MP and bicuculline on orientation and direction sensitivity of a simple cell. Only responses to a moving slit (0.5° x 5°) at the optimal orientation and 90° to it are shown in this figure. Dashed line in each PSTH shows the turning point of the stimulus. Stimulus speed was about 4°/s. Four sweeps for each PSTH, bin width 40 ms. Vertical calibration in C indicates 16 spikes/bin. A control PSTHs made before bicuculline administration. B PSTHs obtained during electrophoretic administration of bicuculline (+60 nA). Records were taken 12–17 min after starting the administration. C control PSTHs made 15–20 min after stopping the bicuculline administration. D PSTHs obtained during intravenous infusion of MP. Records were taken 20–25 min after starting the infusion. E PSTHs obtained during simultaneous administration of both drugs. Records were taken 5–10 min after re-starting bicuculline (+60 nA) in addition to continuous MP infusion, which runs already for 32 min. F control PSTHs made 40–45 min after stopping the administration of both drugs.
GABA-Inh was subsequently found to be insufficient. An alternative explanation is that nerve terminals were stimulated for a longer period of time with bicuculline (1975). This had the effect of stimulating the cells more effectively. This effect was confirmed with similar results on intravenous administration, though the overall loss of inhibition was greater.

The effect of MP on the cells showed some extent of recovery. However, the loss of inhibition was not completely recovered. This is consistent with the complex effect of bicuculline on the cells. The fact that the orientation of the cells was not consistent with bicuculline administration was confirmed in experiments with another cell (1976). A possible explanation for this is that MP and bicuculline may not stimulate the cells in the same way that simple anesthetics would.

Two recent experiments conducted in another laboratory have shown that bicuculline can be used to assemble nerve cells. In these experiments, the cells were isolated at different distances and then the results were recorded. The results were consistent with the hypothesis that bicuculline could be used to establish a novel anesthetic. However, it is important to note that bicuculline inhibition, like MP, is reversible.

The properties of bicuculline are similar to those of MP, but it is more effective. The results of these experiments suggest that bicuculline may be a more suitable anesthetic in certain situations. Further studies are needed to determine the exact mechanisms by which bicuculline works. Nevertheless, bicuculline inhibition appears to be a promising new approach to anesthesia.

Fig. 4. Modification of orientation and direction sensitivity of simple cells by the two drugs. Curves show response magnitude for each cell to a moving slit at testing orientations as indicated on the abscissa. Backward movement of the slit oriented at the optimal, at +90° and at ±45° was represented as +180°, −90° and ±135°, respectively. Number of spikes of spontaneous activity obtained with the same methods as in Fig. 2 are shown on the right. Ordinates indicate total number of spikes in a PSTH. A the same unit as Fig. 3. Continuous line with open circles shows control responses of the cell prior to administration of bicuculline. The other three lines with the symbols as indicated in the top right are obtained from full sets of PSTHs corresponding to Fig. 3B, D, and E. B another simple cell. Symbols are the same as in A. In this cell single application of MP was not made. Results of bicuculline were obtained from a PSTH-set made 12–16 min after starting the electrophoretic ejection (+80 nA). Those of MP + Bic. were obtained 20–24 min after simultaneous application of MP (i.e., at a rate of 15 mg/kg/h and bicuculline electrophoretically +80 nA).
was subthreshold for causing convulsive signs in the EEG, it was probably insufficient to completely inhibit the GABA-synthesizing enzymes. Alternatively, GABA released from presynaptic sites might be taken up by the nerve terminals for re-use, so that gabergic synapses could function for some time without new synthesis of GABA (Iversen, 1971; Storm-Mathisen et al., 1975). These insufficient pre- and postsynaptic effects of the two drugs given alone, may at least partly explain why the combined use of both was more effective than single administration. The fact that electrophoretic MP induced similar, albeit slighter, effects on activities of VC neurons to those by intravenous MP suggests that the latter effects may be at least in part due to a loss of inhibition at the cortical level.

The effects of electrophoretic bicuculline on simple and complex cells is to some extent differential (see Table 1): Reduction or abolishment of the direction sensitivity was seen in 85% of the simple cells, whereas reduction of the orientation sensitivity in 71% of the complex cells. This tendency appears to be consistent with Sillito’s results (1975b, 1977) that the direction sensitivity was lost in simple cells, while the orientation sensitivity was abolished in complex cells. On the other hand, we never observed a complete loss of the orientation sensitivity in complex or simple cells under electrophoretic bicuculline administration. This is in partial disagreement with Sillito’s findings but confirms the observations of Ostendorf and Hess (1975) and Hess et al. (1976). Also, the present results that effects of simultaneous administration of MP and bicuculline was not significantly different in simple and complex cells may not support the dichotomic conclusion that the direction sensitivity of simple and orientation sensitivity of complex cells may be differentially abolished by intracortical disinhibition.

Two reasons might account for the different results obtained in the two laboratories (Hess, personal communication): Firstly, in this laboratory assembled electrodes were used (see methods) in contrast to multibarrelled pipettes because of their better recording properties. The different electrode distances might to some extent affect the distribution of drugs in relation to the recorded nerve cell and thus lead to different results. The second and more likely possibility is the influence of anaesthetics. While Sillito used nitrous oxide in his experiments, we worked on Nembutal anaesthetized animals. As Nembutal reduces central excitability and possibly enhances GABA-mediated inhibition, it might also reduce the effectiveness of electrophoretically applied BIC.

The present findings that orientation and direction sensitivity of VC neurons could be nearly completely abolished by the two simultaneously administered drugs which interfer with gabergic inhibition supports the suggestion that these properties depend on intracortical inhibition (Creutzfeldt and Iso, 1968; Benevento et al., 1972; Creutzfeldt et al., 1974). The fact that the response to the optimal stimulus was increased by disinhibition as well, is also consistent with the model based on intracellular recordings from VC neurons (Creutzfeldt et al., 1974). Furthermore, responsive areas were virtually round during blockade of gabergic inhibition, as also suggested by intracellular recordings (Creutzfeldt et al., 1974) as well as by the response width in non-optimal
orientations during glutamate excitation (Hess and Murata, 1974). It is therefore reasonable to conclude that intracortical inhibition makes visual cortical neurons more or less selectively responsive to moving line stimuli of certain orientation and direction. It remains still a riddle, however, why the inhibitory mechanism responsible for orientation sensitivity appears to be more resistant to removal of gabergic inhibition than that for direction sensitivity. The stronger resistance of orientation sensitivity to disinhibition may indicate that the input to cortical neurons already has an orientational bias as suggested by recordings in the retina (Hammond, 1974) and the lateral geniculate body (Cereuzfeldt and Nothdurft, 1978). The fact that some neurons are not affected at all by either drug, suggests that at least some of them may be second order cortical neurons, which are driven by orientation/direction sensitive first order neurons.

Acknowledgements. W. Eckart, who developed the computer programs and collaborated in the design and performance of the experiments, died in September 1977, 6 months after completion of the experimental work. We gratefully acknowledge his ingenious and inventive contributions. We also thank Drs. R. Hess and B.B. Lee for helpful advice during the experiments and preparation of the manuscript.

References


Pettigrew, J.D., Daniels, J.D.: GABA antagonism in visual cortex: different effects on simple, complex, and hypercomplex neurones. Science 182, 81–83 (1973)


Silvio, A.M.: The contribution of inhibitory mechanisms to the receptive field properties of neurones in the striate cortex of the cat. J. Physiol. (Lond.) 250, 305–329 (1975b)


Tsumoto, T.: Inhibitory and excitatory binocular convergence to visual cortical neurons of the cat. Brain Res. (in press)


Received June 22, 1978