Proc. Natl. Acad. Sci. USA
Vol. 85, pp. 3623–3627, May 1988
Neurobiology

Neural plasticity without postsynaptic action potentials: Less-active inputs become dominant when kitten visual cortical cells are pharmacologically inhibited

(visual cortex/central nervous system development/Hebb synapse/activity-dependent plasticity/monocular deprivation)

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Communicated by Torsten N. Wiesel, December 9, 1987 (received for review July 10, 1987)

ABSTRACT **Models of synaptic plasticity in the nervous system have conventionally assumed a mechanism in which spike activity of a postsynaptic cell enhances the efficacy of recently active presynaptic inputs. Making use of the prompt and dramatic response of the visual cortex to occlusion of vision in one eye during the critical period, we tested the role of postsynaptic activity in ocular dominance plasticity. To do so, we selectively blocked cortical cell discharges with a continuous intracortical infusion of the inhibitory neurotransmitter agonist muscimol during a period of monocular deprivation. This drug inhibits cortical cell discharges with no apparent effect on the activity of their presynaptic geniculocortical inputs. Recording from single cortical cells after they had recovered from the muscimol-induced blockade, we found a consistent shift in the responsiveness of the visual cortex in favor of the less-active, *closed eye*, while the normal shift in favor of the more-active, open eye was evident in regions not affected by the treatment. Such an inhibition-coupled expression of plasticity in favor of the less-active, closed eye cannot be explained by a nonspecific disruption of cortical function. We interpret these results to indicate (*i*) that the postsynaptic cell is crucially involved in plasticity of the visual cortex, (*ii*) that the direction of cortical plasticity depends on postsynaptic membrane conductance or polarization, and (*iii*) that plasticity can occur in the absence of postsynaptic spike activity.**

Synaptic plasticity is known to be widespread in both the developing and the mature central nervous system. A hypothesis about the mechanism of plasticity in development, put forward by Hebb, is that spike activity in the postsynaptic cell enhances the efficacy of recently active inputs (1–6). Hebb's hypothesis has been used to explain many instances of neural plasticity (7). This hypothesis stands in contrast to one favoring a purely presynaptic mechanism, as was reported for classical conditioning in *Aplysia*, in which responses of cells were facilitated even while their somata were hyperpolarized by an intracellular microelectrode (8). In the visual (9–14) and motor cortices (15), however, several types of evidence favor an excitation-coupled postsynaptic mechanism of plasticity.

Synaptic connections serving the two eyes to the visual cortex are reorganized during normal development (16–18). This reorganization is most dramatic when vision in one eye is occluded during a critical period in early life (17–20): the occluded eye loses its ability to drive most cortical cells, which come to respond exclusively to the nonoccluded eye. This phenomenon is called ocular dominance plasticity.

Previous experiments in which a region of visual cortex was infused with tetrodotoxin during a period of monocular deprivation demonstrated that activity at the level of the visual cortex is crucial for ocular dominance plasticity (10). Because tetrodotoxin blocks pre- as well as postsynaptic activities in the visual cortex, these experiments could not answer the question as to which elements in the cortex must be active for plasticity to occur. A logical approach to answering this question is to block just the postsynaptic elements involved in cortical synaptic plasticity. Because the neurotransmitter(s) used by the geniculocortical afferents are not known, we were unable to selectively block the postsynaptic effects of geniculocortical transmission. Instead, we emulated the *Aplysia* experiments of Carew *et al.* (8) and inhibited postsynaptic cortical neurons under circumstances in which, were these cells not inhibited, we would have expected plasticity. Unlike the *Aplysia* studies, in which inhibition was produced by an intracellular microelectrode, in the present experiments kitten cortical cells were inhibited pharmacologically. If the postsynaptic spike activity were a crucial element of the mechanism underlying ocular dominance plasticity, then we would expect that selective blockade of this activity should prevent such plasticity.

To block postsynaptic activity selectively, we used the drug muscimol, an agonist of the inhibitory neurotransmitter γ-aminobutyric acid (GABA) that is selective for the GABA-A receptor. GABA is the principal inhibitory neurotransmitter in cerebral cortex (21, 22); GABA is found in all layers (23) and powerfully inhibits all, or nearly all, neurons (24). Although the inhibitory action of GABA is generally associated with a direct postsynaptic effect (25), GABA has also been shown to have a presynaptic effect—namely, that of reducing neurotransmitter release from presynaptic nerve terminals (26–28). In all cases, however, this activity has been shown to be mediated through the GABA-B receptor, at which muscimol and other GABA agonists, such as 4,5,6,7-tetrahydroisoxazolo[5,4-*c*]pyridine-3-ol and 3-aminopropane sulfonic acid, are not, or are only minimally, active (26–28). In addition, muscimol binding can always be antagonized by bicuculline, a GABA antagonist active at the GABA-A binding site, whereas the effects associated with binding to the GABA-B receptor are completely or largely bicuculline-insensitive (25–28). In the kitten visual cortex, GABAergic inhibition is already present (29–31), and muscimol appears to bind *only* to GABA-A receptors (32, 33).

MATERIALS AND METHODS

We stereotaxically implanted a 33-gauge stainless steel cannula (o.d. 200 μm) connected to a 0.5-ml/hr osmotic minipump (Alza model 2002) containing 10 mM muscimol (Sigma) in sterile saline into the right visual cortex of eight

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Abbreviations: GABA, γ-aminobutyric acid; CBI, contralateral bias index.

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normal 27- to 32-day-old kittens. In preliminary experiments the effects of muscimol were tested in six otherwise normal cats and kittens; we measured the onset and time of activity of the drug and the resulting areas of blockade. These experiments showed cortical receptive fields and levels of responsiveness to be normal after an appropriate drug wearing-off period, whereas the blockade extended at least 2 mm anterior to the cannula after 2 days of drug infusion. Therefore we allowed 3 days of drug infusion for the blockade to reach steady state before occluding vision in one eye for 5–7 days. Following an 8- to 11-day period of intracortical infusion, including 5–7 days of monocular deprivation, the animals were prepared for single-unit recording using standard techniques (10).

During the course of a 32- to 40-hr experiment, we made microelectrode recordings in the following sequence: (*i*) We determined the size of the area in which cortical cell discharges were blocked by the muscimol infusion, (*ii*) we disconnected the minipump to stop the infusion and allow the cortex to recover its responsiveness, (*iii*) we made recordings in unaffected control areas, and (*iv*) after the recovery, we made recordings in the previously blocked area. These recordings focused on the ocular dominance of the cortical neurons, but orientation selectivity, degree of habituation, and overall responsiveness were also noted. These response properties were compared to those previously recorded (10) near identical cannulae in three additional control kittens that were infused with a buffered vehicle solution.

A blind procedure was used for the latter half of the experiments to ensure that the results were not biased by the experimenter's knowledge of the side of the eyelid closure. Under this procedure, the eyelid suture and the first day's recording were done by the first experimenter, who altered the appearance of the nondeprived eye in such a manner that the second experimenter could not tell which eye had been previously closed, delineated the region of blockade, made recordings in unblocked control areas, and directed the second experimenter to limit the second day's recording to the region of blockade. Results from control areas were not disclosed to the second experimenter until after completion of all recordings.

RESULTS

During the recording portion of the experiment, we first assessed size of the cortical blockade in each animal by making several vertical extracellular microelectrode penetrations at increasing distances from the cannula. The blocked area was delineated by penetrations in which no visually evoked activity could be recorded from cortical cells within 2 mm of the pial surface; in most such penetrations, only injury discharges, or no discharges at all, were recorded. The first signs of cortical responsiveness to visual stimulation located a partially blocked area anterior to the complete blockade. Recordings within both blocked and partially blocked regions revealed no effect of the muscimol treatment on the electrical activity of the geniculocortical afferent terminals. Afferent discharges were indeed so vigorous and easily recorded that their locations reliably predicted the exact anatomical borders of layers IV and VI. Subsequent examinations of Nissl-stained sections revealed no anatomical abnormalities as a result of the muscimol treatment except for physical damage at the site of the cannula.

After assessment of size of the blocked area, the cannula was disconnected from the minipump to allow the cortex to recover its responsiveness. During this recovery period, several more electrode penetrations were made in unaffected anterior regions of the muscimol-treated side and/or the contralateral control hemisphere in order to assess the effect of the monocular deprivation in control regions. This effect was assessed by recording from single neurons and determining the relative strength of the two eyes' inputs according to the Hubel–Wiesel seven-point scale (34). The ocular dominance histograms from the control areas are shown in Fig. 1 *c* and *d*; Fig. 1*c* shows the expected shift in favor of the open eye for an example (kitten 530), whereas Fig. 1*d* shows a similar shift for the group data compiled from the control regions of all eight experimental animals.

By 20–26 hr after discontinuing the muscimol infusion, during which the animals remained anesthetized, neurons in the previously blocked area had regained remarkably normal

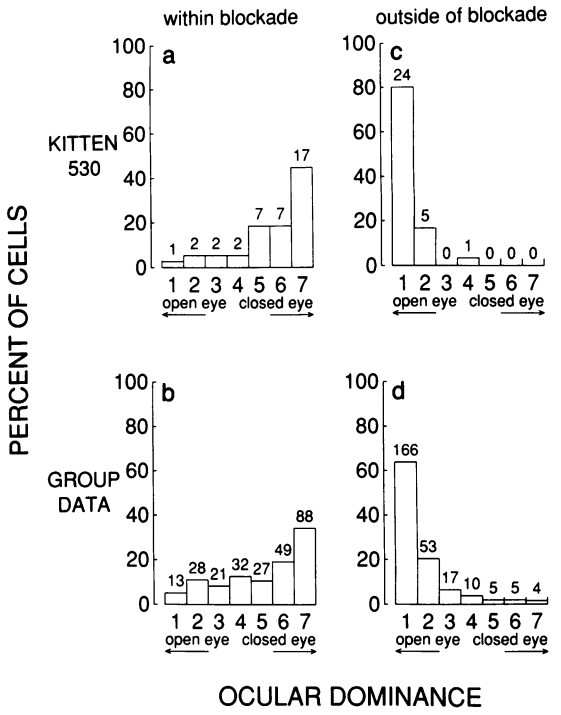

FIG. 1. Ocular dominance histograms (34) compiled from single-unit responses in area 17. Monocular eyelid closures were done in different animals, either ipsilateral or contralateral to the muscimol-infused hemisphere. Results are plotted as if the eyelid sutured was always ipsilateral to the treated hemisphere, and control recordings were obtained from unaffected regions of that hemisphere. That is, responses from single cells were plotted such that an ocular dominance of 1 indicates a cell driven only by the **open** eye; ocular dominance of 7 indicates a cell driven only by the **closed** eye; and ocular dominance of 4 indicates a cell driven equally by the two eyes. All animals received intracortical muscimol infusions for 8–10 days and were monocularly deprived for 5–7 days. The direction of ocular dominance shift within the area blocked by the muscimol infusion was the same in all animals tested and opposite to the direction of shift in control areas outside the blockade. (*a*) Thirty-eight visually responsive units recorded within the muscimol-blocked area in kitten 530 (data also shown in Fig. 2*c*) reveal a shift of the ocular dominance distribution in favor of the **closed** eye. (*c*) Thirty visually responsive units recorded outside of the muscimol-blocked area in kitten 530 (in this case, in the hemisphere contralateral to the muscimol-infused hemisphere) show the normally observed shift of the ocular dominance distribution in favor of the **open** eye (18). (*b*) Two hundred fifty-eight visually responsive units recorded in seven of the eight experimental kittens (excluding kitten 525 as the size of the blockade was not measured in this animal—see Fig. 2*b*). (*d*) Two hundred and sixty visually responsive units recorded in the eight experimental kittens in areas outside of the muscimol-induced blockade (areas include contralateral control hemisphere as well as unaffected areas anterior to the muscimol-induced blockades; histogram includes cells recorded in the contralateral control hemisphere of kitten 525, but not units recorded anterior to the presumably blocked region on the muscimol infusion side).

responses to visual stimulation. Only 5% of these neurons displayed no selectivity for orientation, and an additional 16% were poorly selective or only biased for orientation. The corresponding figures in the control animals were 2% and 11%, respectively. Strong habituation was evident in 28% of neurons in the previously blocked area as compared with 23% in control kittens. Visual responsiveness increased over the course of these recordings, presumably as the muscimol continued to diffuse out of the treated area. The majority of these neurons displayed the same vigor of responsiveness as is found in normal cortex.

Ocular dominance histograms were then compiled from penetrations within the area that was previously completely blocked. Fig. 1*a*, for the same example, and Fig. 1*b*, for the group data compiled from seven animals (see figure legend), show that the ocular dominance distribution shifted in favor of the less-active, **closed eye** within the previously blocked regions.

Surprised by these results from an initial group of four animals, we repeated the experiment on another four kittens using a "blind" experimental procedure so that one of us did not know which eye had been deprived. Fig. 2 illustrates the shift in ocular dominance in relation to the area of the blockade for each of the eight animals studied. Fig. 2*c* plots results from the kitten whose ocular dominance histograms are shown in Fig. 1 *a* and *c*. The ocular dominance distribution of the units encountered in each penetration was summarized by a single number, the contralateral bias index (CBI). Each point in the panels plots the difference between the CBI value expected for a normal, untreated cortex and the CBI value calculated for the penetration at the indicated distance from the cannula. Ocular dominance shifts in favor of the closed eye are plotted as negative numbers, whereas shifts in favor of the open eye are plotted as positive numbers. This figure shows that the results from the experiments conducted according to the nonblind procedure (*Left*) are virtually identical to the results obtained using the modified, blind procedure (*Right*).

The results from each animal showed the same tendency: a shift in favor of the **closed eye** close to the cannula, within

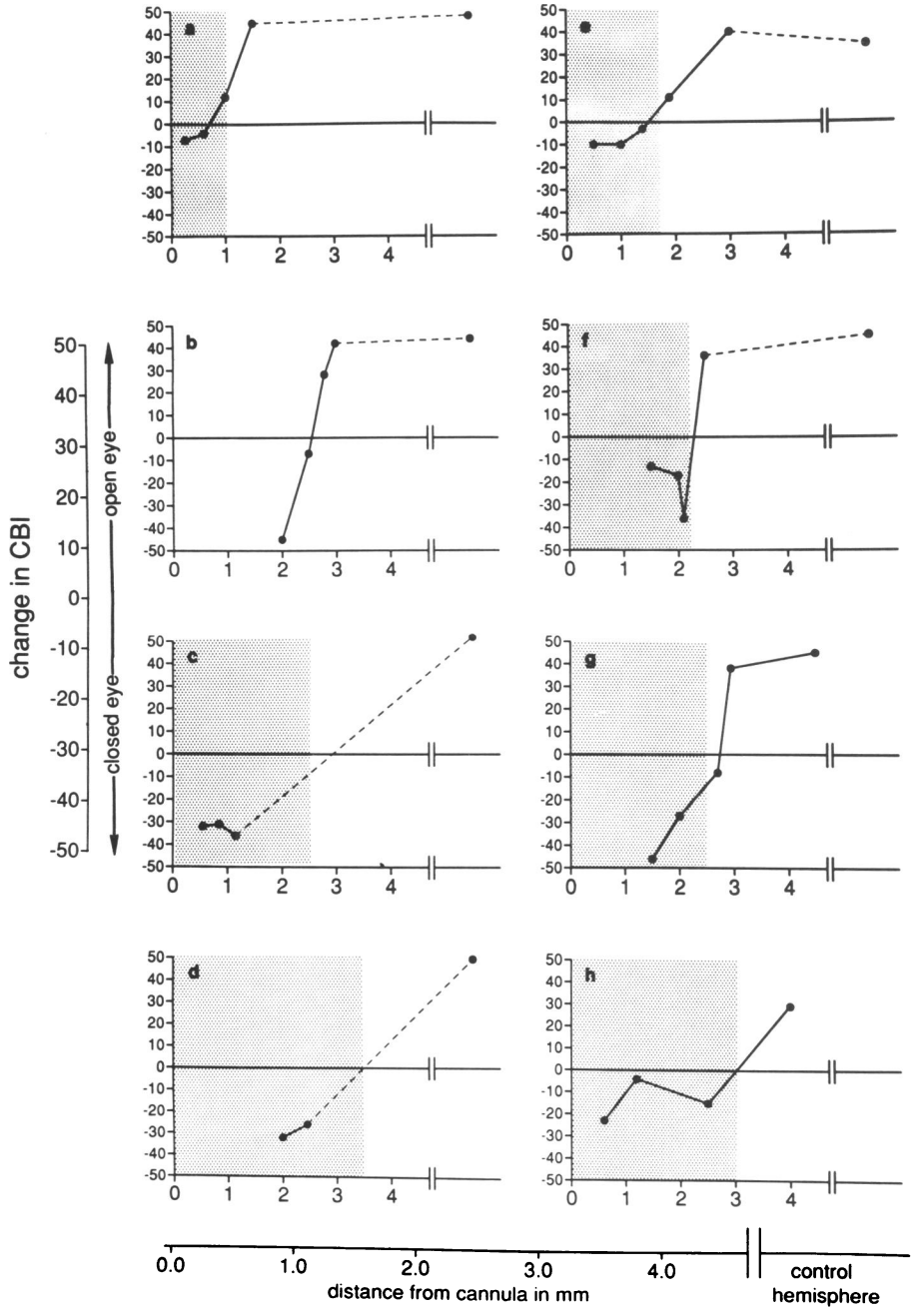

FIG. 2. Changes in the CBI calculated for units in each individual penetration (●) at locations defined with respect to the infusion site. CBI = 100[(**1** − **7**) + 2/3(**2** − **6**) + 1/3(**3** − **5**) + *n*]/2*n*. Boldface numbers, number of units in each ocular dominance group; *n*, total number of visually responsive units. This index is 100 if all cells are driven exclusively by the contralateral eye and 0 if all cells are driven exclusively by the ipsilateral eye. The CBI of normal kittens is about 55 on account of the naturally slight bias in favor of the contralateral eye (35). Therefore, we took a CBI of 55 as our baseline (zero line in the panels) and calculated the difference between 55 and the CBI value for each penetration. In cases of contralateral eyelid sutures (*b*, *e*, and *h*), the difference was still plotted as a negative value—i.e., one showing a shift in favor of the **closed** eye. Representative *x*- and *y*-axes for all eight plots are shown at the bottom and to the left of the panels. ●—●, change in CBI values for penetrations within the muscimol-treated hemisphere; ●---●, change in CBI values for penetrations in the contralateral control hemisphere. Gray areas in each panel illustrate the size of the muscimol-induced blockade of cortical neurons rostral to the location of the implanted cannula. (*b*) (kitten 525) does not display this gray area, because the cannula was disconnected before assessment of the blocked area. Four animals (*e–h*) were tested using a blind procedure (see text). The data from all animals share the following characteristics: (*i*) a shift in the ocular dominance distribution in favor of the **closed** eye near the cannula, within the region previously blocked by the muscimol infusion, (*ii*) an opposite shift in favor of the open eye near the border or outside of the blocked area and/or in the contralateral control hemisphere, and (*iii*) a change in the ocular dominance distribution from favoring the closed eye to favoring the open eye always occurs at or near the border of the area in which the activity of cortical neurons had been completely blocked by the muscimol infusion.

the region previously blocked by muscimol, and an opposite shift in favor of the open eye farther from the cannula, in partially affected and unaffected control regions. The size of the blocked area appeared to be related to the degree of shift of ocular dominance. This relation is illustrated in Fig. 3, which shows (□, ····) that the animals with the small areas of blockade (<1.7 mm—Fig. 2 *a* and *e*) displayed the least bias in ocular dominance in favor of the closed eye, while animals with blockades exceeding 2.2 mm (Fig. 2 *c*, *d*, and *f–h*) show considerable shifts in favor of the closed eye (correlation coefficient, $r = 0.674$). We interpret the size of the blockade to be related to the effective concentration of muscimol present during the period of monocular deprivation and, hence, to the degree of inhibition induced by the muscimol treatment. Thus, this relation suggests that the more inhibited the cortical neurons were during the period of monocular deprivation, the stronger was the shift in favor of the closed eye. The size of the muscimol-blocked area was also closely related to the distance from the cannula at which the ocular dominance shift reversed from favoring the closed eye to favoring the open eye. This relationship is also shown in Fig. 3 (●, —) for the five animals (Fig. 2 *a* and *e–h*) in which recordings were made just posterior and anterior to the previously blocked areas. The correlation coefficient for this relation is $r = 0.989$.

DISCUSSION

These results show that the postsynaptic neurons are crucially involved in ocular dominance plasticity. This is evident from the fact that the identical geniculocortical input activities, caused by monocular deprivation, can shift ocular dominance to favor either the open or closed eye, depending entirely on the state of the postsynaptic cortical neuron (that is, either unaffected by muscimol and therefore depolarizable, producing a shift toward the open eye, or affected by muscimol and therefore inhibited—probably shunted—producing a shift toward the closed eye). The present findings do not resolve whether the ocular dominance shift seen in favor of the closed eye results, at a synaptic level, from a strengthening of that eye's inputs to cortical cells at the expense of inputs from the open eye or whether, instead, it is caused solely by a weakening of the inputs from the open eye. Therefore, it would be equally reasonable at this point to describe the findings as a shift in ocular dominance away from the more active, open eye.

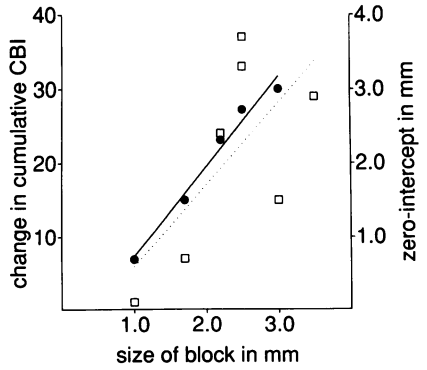

FIG. 3. Combined plot of the change in cumulative CBI (as defined in legend for Fig. 2) in the seven animals in which the size of the blockade was assessed before disconnecting the cannula (Fig. 2 *a* and *c–h*, □ and ····) and of the zero intercepts (distance from the cannula at which the ocular dominance shift reversed direction) in the five animals in which both properties had been assessed (Fig. 2 *a* and *e–h*, ● and —), as a function of the size of the muscimol-induced blockade of cortical neuron activity. The change in cumulative CBI was calculated for each animal from the single-unit data of all penetrations within formerly blocked cortex. Straight lines determined by linear regression have a correlation coefficient of $r = 0.674$ (····) and of $r = 0.989$ (—).

A potential problem with the interpretation that the state of postsynaptic cortical neurons determines the direction of plasticity would exist were muscimol to have a presynaptic effect as well. While this possibility cannot be excluded entirely, several lines of evidence suggest that this is not so. First, our microelectrode recordings revealed no evidence of a blocking effect on the electrical activity of the geniculate afferents. Second, muscimol-binding studies (32, 33) demonstrate binding in kitten visual cortex with a single binding affinity and GABA-A pharmacology. Third, although binding of GABA to pre- and postsynaptic GABA-B receptors has also been demonstrated (25–27), the effects of muscimol binding to GABA-A receptors and GABA- or baclofen-binding to GABA-B receptors clearly seem to operate through different mechanisms (25–27, 36). Finally, if the muscimol treatment, contrary to the available evidence, were to have an effect on either presynaptic transmission or neurotransmitter release, this effect would serve to obscure the monocular deprivation effect and therefore counteract the expression of plasticity. The plasticity observed in the muscimol-treated kittens, however, is incompatible with a muscimol effect on either presynaptic transmission or neurotransmitter release. Thus, it is unlikely that muscimol treatment of visual cortex affects the normal transmission of and neurotransmitter release from presynaptic geniculocortical afferent terminals. The plasticity in favor of the closed eye strongly argues against nonspecific effects, which presumably would interfere with the mechanisms that allow plasticity.

The interpretation that muscimol treatment alters ocular dominance plasticity solely by its effects on postsynaptic cortical cells is potentially complicated by the presence of corticosubcortical feedback, which could modify the presynaptic geniculocortical inputs to the treated area. Two observations indicate that such subcortical effects do not account for the present results. First, we recorded from geniculocortical afferents in the presence of muscimol and found them to be normally responsive. Second, and more importantly, activity in corticosubcortical pathways is identically blocked by cortical infusions of muscimol and tetrodotoxin (10), whereas the ocular dominance shifts that result from these two manipulations are quite different.

The present results also suggest that the direction of cortical plasticity is controlled by postsynaptic membrane voltage or conductance. This suggests the following type of "learning-rule" for ocular dominance plasticity: the connections between the more-active open eye inputs and strongly inhibited postsynaptic cells are weakened relative to the inputs from the less-active closed eye, while the reverse happens when the postsynaptic cells are not inhibited completely. This learning rule suggests the presence of a threshold membrane potential that determines the direction of an ocular dominance shift. Further work will be required to determine whether the hypothesized learning rule is part of normal development.

A final conclusion from our results is that ocular dominance plasticity can occur in the absence of postsynaptic spike activity, suggesting that at least this form of plasticity is controlled by a mechanism related to the state of the postsynaptic conductance or membrane potential. The fact that plasticity was maintained in the absence of postsynaptic spike activity argues very strongly in favor of this interpretation. The necessity of a substantial postsynaptic inhibition for this form of plasticity—the ocular dominance shift in favor of the closed eye—is supported by three observations. (*i*) Recording in areas bordering the completely blocked regions revealed shifts toward the open eye. This border area was clearly affected by the muscimol treatment, and was

nearly, though not completely, incapable of responding to visual stimulation with action potentials. (*ii*) Tetrodotoxin infusion into cortex, presumably by blocking depolarization only, merely prevents ocular dominance plasticity (10), but does not produce a shift in favor of the closed eye. (*iii*) The magnitude of the ocular dominance shift toward the closed eye was smaller in the animals with smaller regions of blockade (Fig. 2 *a* and *e*, and Fig. 3).

The first observation of the previous paragraph also suggests that the normal ocular dominance shift–in favor of the more-active, open eye–does not require postsynaptic spike activity. In border regions, in which postsynaptic spike activity was nearly, but not completely, eliminated during the period of deprivation, this shift was nearly as strong as in untreated cortex.

Surprising as plasticity in favor of the less-active, closed eye may appear, it is known that the levels of several biochemical markers are also relatively increased in territory dominated by less-active inputs. Hendry and Kennedy (37) have reported cytochemical evidence for increases in the level of type II Ca^{2+}/calmodulin-dependent protein kinase in neurons in deprived eye columns in monocularly enucleated or deprived monkeys. Graybiel and Ragsdale (38) have found that butyryl- and acetylcholinesterase levels are also higher in regions of visual cortex deprived of input by unilateral enucleation. In culture systems as well, reductions in electrical activity may increase the expression of some neurotransmitter systems (39).

On the evidence presented here, we hypothesize that ocular dominance plasticity is regulated by a combination of excitation- and inhibition-coupled mechanisms that crucially involve the state of conductance of the postsynaptic cortical cells. Therefore, these data provide direct evidence in support of the part of Hebb's postsynaptic model that suggests a crucial role for the postsynaptic element. Because plasticity in favor of the closed eye clearly occurs in the absence of postsynaptic spike activity, and the excitation-coupled plasticity in favor of the open eye can occur in regions in which postsynaptic spike activity is profoundly attenuated, we suggest that, contrary to Hebb's postulate, local responses rather than action potentials govern cortical plasticity.

We are grateful to Z. Hall, A. J. Hudspeth, S. G. Lisberger, and R. A. Nicoll for comments on an earlier version of this manuscript. This work was supported by grants from the National Institutes of Health, McKnight Foundation, and University of California Academic Senate.

1. Stent, G. (1973) *Proc. Natl. Acad. Sci. USA* **70,** 997–1001.
2. Changeux, J.-P. & Danchin, A. (1976) *Nature (London)* **264,** 705–712.
3. Rauschecker, J. P. & Singer, W. (1981) *J. Physiol. (London)* **310,** 215–239.
4. Willshaw, D. J. & von der Malsburg, C. (1977) *Proc. R. Soc. London Ser. B* **194,** 431–445.
5. Hebb, D. O. (1949) in *The Organization of Behavior* (Wiley, New York).
6. Bienenstock, E. L., Cooper, L. N. & Munro, P. W. (1982) *J. Neurosci.* **2,** 32–48.
7. Collingridge, G. L. & Bliss, T. V. P. (1987) *Trends Neurosci.* **10,** 288–293.
8. Carew, T. J., Hawkins, R. D., Abrams, T. W. & Kandel, E. R. (1984) *J. Neurosci.* **4,** 1217–1224.
9. Shaw, C. & Cynader, M. (1984) *Nature (London)* **308,** 731–734.
10. Reiter, H. O., Waitzman, D. M. & Stryker, M. P. (1986) *Exp. Brain Res.* **65,** 182–188.
11. Kasamatsu, T. & Pettigrew, J. D. (1976) *Science* **194,** 206–208.
12. Bear, M. F. & Singer, W. (1986) *Nature (London)* **320,** 172–176.
13. Fregnac, Y. & Imbert, M. (1984) *Physiol. Rev.* **64,** 325–434.
14. Fregnac, Y. (1987) in *Imprinting and Cortical Plasticity*, eds. Rauschecker, J. & Marler, P. (Wiley, New York), pp. 221–266.
15. Baranyi, A. & Feher, O. (1981) *Neurosci. Lett.* **23,** 303–308.
16. Hubel, D. H., Wiesel, T. N. & LeVay, S. (1977) *Phil. Trans. R. Soc. London Ser. B* **278,** 131–163.
17. LeVay, S. & Stryker, M. P. (1979) in *Aspects of Developmental Neurobiology (Soc. Neurosci. Symp.)*, ed. Ferrendelli, J. A. (Soc. Neurosci., Bethesda, MD), pp. 83–98.
18. Shatz, C. J. & Stryker, M. P. (1978) *J. Physiol. (London)* **281,** 267–283.
19. LeVay, S., Wiesel, T. N. & Hubel, D. H. (1980) *J. Comp. Neurol.* **191,** 1–51.
20. Wiesel, T. N. & Hubel, D. H. (1963) *J. Neurophysiol.* **26,** 1003–1017.
21. Iversen, L. L., Mitchell, J. F. & Srinivasan, V. (1971) *J. Physiol. (London)* **212,** 519–531.
22. Krnjevic, K. & Schwartz, S. (1967) *Exp. Brain Res.* **3,** 320–336.
23. Hendrickson, A. E., Hunt, S. P. & Wu, Y.-P. (1981) *Nature (London)* **292,** 605–607.
24. Hess, R. & Murata, K. (1974) *Exp. Brain Res.* **21,** 285–297.
25. Newberry, N. R. & Nicoll, R. A. (1985) *J. Physiol. (London)* **360,** 161–185.
26. Bowery, N. G., Hill, D. R., Hudson, A. L., Doble, A., Middlemiss, D. N., Shaw, J. & Turnbull, M. (1980) *Nature (London)* **283,** 92–94.
27. Hill, D. R. & Bowery, N. G. (1981) *Nature (London)* **290,** 149–152.
28. Bowery, N. G. (1982) *Trends Pharmacol. Sci.* **3,** 400–403
29. Tsumoto, T. & Sato, H. (1985) *Vision Res.* **25,** 383–388.
30. Shaw, C., Needler, M. C. & Cynader, M. (1984) *Brain Res. Bull.* **13,** 331–334.
31. Wolf, W., Hicks, T. P. & Albus, K. (1986) *J. Neurosci.* **6,** 2779–2795.
32. Needler, M. C., Shaw, C. & Cynader, M. (1984) *Brain Res.* **308,** 347–353.
33. Skangiel-Kamska, J. & Kossut, M. (1984) *Acta Neurobiol. Exp.* **44,** 33–39.
34. Hubel, D. H. & Wiesel, T. N. (1962) *J. Physiol. (London)* **160,** 106–154.
35. Stryker, M. P. & Harris, W. A. (1986) *J. Neurosci.* **12,** 2117–2133.
36. Waddington, J. L. & Cross, A. J. (1979) *Naunyn-Schmiedeberg's Arch. Pharmacol.* **306,** 275–280.
37. Hendry, S. H. C. & Kennedy, M. B. (1986) *Proc. Natl. Acad. Sci. USA* **83,** 1536–1540.
38. Graybiel, A. M. & Ragsdale, C. W., Jr. (1982) *Nature (London)* **299,** 439–442.
39. Black, I. B., Adler, J. E., Dreyfus, C. F., Friedman, W. F., LaGamma, E. F. & Roach, A. H. (1987) *Science* **236,** 1263–1268.