

ways in the brainstem which are involved in central regulation of parasympathetic function. In previous experiments we found that the response to GABA antagonists was not altered by a midcollicular transection (7), which suggests that the mechanisms involved in this response are located within the hindbrain. Whether GABA is released from the terminals of neurons intrinsic to the nucleus ambiguus, or from neurons projecting to this nucleus from more distant sites in the brainstem, it appears likely that GABA, by interacting with receptors on neurons in the nucleus ambiguus, may inhibit parasympathetic outflow to the heart.

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References and Notes

1. G. A. R. Johnston, in *GABA in Nervous System Function*, E. Roberts, T. H. Chase, D. B. Tower, Eds. (Raven, New York, 1976), p. 395; S. J. Enna, J. F. Collins, S. H. Snyder, *Brain Res.* **124**, 185 (1977); K. Beaumont, W. S. Chilton, H. I. Yamamura, S. J. Enna, *ibid.* **148**, 153 (1978); P. Krosgaard-Larsen, G. A. R. Johnston, D. A. Curtis, C. J. A. Game, R. M. McCulloch, *J. Neurochem.* **25**, 803 (1975).
2. L. Grandison and A. Guidotti, *Neuropharmacology* **16**, 533 (1977).
3. J. Scheel-Kruger, A. R. Cools, W. Honig, *Eur. J. Pharmacol.* **42**, 311 (1977); J. Scheel-Kruger, J. Arnt, G. Magelund, *Neurosci. Lett.* **4**, 351 (1977).
4. K. Gale and A. Guidotti, *Nature (London)* **263**, 691 (1976); G. Zsilla, D. L. Cheney, E. Costa, *Naunyn-Schmiedeberg's Arch. Pharmacol.* **294**, 251 (1976); K. Fuxe, T. Hokfelt, L. Agnati, O. Johansson, A. Ljungdahl, M. Perez de la Mora, *Adv. Biochem. Psychopharmacol.* **16**, 47 (1977).
5. L. Grandison and A. Guidotti, *Fed. Proc. Fed. Am. Soc. Exp. Biol.* **37**, 555 (1978); E. Vijayan and S. M. McCann, *ibid.*, p. 555; M. Simonovic, H. Y. Meltzer, V. S. Fang, *ibid.*, p. 555.
6. M. J. Antonaccio and D. G. Taylor, *Eur. J. Pharmacol.* **46**, 283 (1977); M. J. Antonaccio, L. Kerwin, D. G. Taylor, *7th International Congress of Pharmacology* (Paris, 1978), Abstr. 2068. Similar results were recently reported by B. Delbarre and D. Senon [*11th Collegium Internationale Neuro-psychopharmacologicum (CINP) Congress* (Vienna, 1978), p. 39] after intracerebroventricular application of diazepam.
7. J. A. DiMicco, B. L. Hamilton, R. A. Gillis, *J. Pharmacol. Exp. Ther.* **203**, 64 (1977); J. A. DiMicco and R. A. Gillis, *ibid.*, in press; *Fed. Proc. Fed. Am. Soc. Exp. Biol.* **37**, 687 (1978).
8. A. Guidotti, in *Psychopharmacology: A Generation of Progress*, M. A. Lipton, A. DiMascio, K. F. Killam, Eds. (Raven, New York, 1978); E. Costa, A. Guidotti, G. Toffano, *Br. J. Psychiatry*, in press; E. Costa, A. Guidotti, C. C. Mao, in *GABA in Nervous System Function*, E. Roberts, T. H. Chase, D. B. Touge, Eds. (Raven, New York, 1976), p. 413.
9. C. H. Hoekman and K. E. Livingston, *Neuropharmacology* **12**, 319 (1973); J. A. Quest, L. S. Freer, J. R. Kunec, R. A. Gillis, *Life Sci.* **21**, 659 (1977).
10. C. G. Gunn, G. Sevelius, M. J. Puiggari, F. K. Myers, *Am. J. Physiol.* **214**, 258 (1968); R. M. McAllen and K. M. Spyer, *J. Physiol. (London)* **258**, 187 (1976); H. I. Chen and C. Y. Chai, *Am. J. Physiol.* **231**, 454 (1976); N. K. Achari, C. B. B. Downman, W. V. Weber, *J. Physiol. (London)* **197**, 35P (1968); F. R. Calaresu, A. A. Faiers, G. J. Mogenson, *Prog. Neurobiol. (N.Y.)* **5**, 1 (1975).
11. Y. Miyata, K. Obata, Y. Tanaka, M. Otsuka, *J. Physiol. Soc. Jpn.* **32**, 377 (1970).
12. A. L. Berman, *The Brain Stem of the Cat* (Univ. of Wisconsin Press, Madison, 1968).
13. The rate of infusion was found to be critical, as infusion of saline at rates higher than those used in the present study often elicited profound bradycardia. These artifacts, presumably due to mechanical stimulation [see H. I. Chen and C. Y. Chai in (10)], were excluded in the present study by (i) placing the cannula at least 5 minutes before drug injection, and (ii) testing the effects of saline infusion at the same rates used for drug injection.
14. D. L. Kunze, *J. Physiol. (London)* **222**, 1 (1972).
15. Supported by grant NS-12566 from the Public Health Service.

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Alteration of Cortical Orientation Selectivity: Importance of Asymmetric Input

Abstract. Rearing cats so that each of the two eyes sees stripes of a different orientation alters the orientation preference of visual cortex cells. This result can be obtained by rearing the cats in striped cylinders or with goggles attached to their faces, but a tighter control of orientation preference is achieved by the goggles.

In normal cats the orientation preferences of single units in visual cortex are uniformly distributed (1). Blakemore and Cooper reported that rearing animals in horizontally or vertically striped cylinders altered this distribution (2). Most of the cells in the visual cortex preferred stimuli with the orientation seen during rearing. This finding has been replicated in both Blakemore's (3) and Pettigrew's (4) laboratories, but Stryker and Sherk have failed to replicate it (5). Stryker and Sherk found a uniform distribution of preferred orientations in animals reared in striped cylinders. Hirsch and his colleagues have altered the distribution of preferred orientations by rearing cats wearing striped goggles; one eye saw vertical stripes and the other eye saw horizontal stripes (6). This procedure controlled the orientation preferences of cortical cells with great precision so that even cells preferring diagonals were extremely rare. Stryker *et al.* (7) confirmed and extended this result.

Because there have been no detailed reports comparing cylinder- and goggle-reared animals from the same laboratory, it is difficult to determine whether goggle rearing is, in fact, substantially more effective at shaping cell properties than cylinder rearing. There are at least two important differences between the two rearing procedures. (i) In animals reared with goggles, the orientation of stripes on the retina is practically constant, the only changes being those due to torsional eye movements. In contrast, in animals reared in cylinders, the orientation of stripes on the retina changes when the animal tilts his head or when he looks at the distant top or bottom of the cylinder. (ii) The effects of symmetric input (both eyes seeing the same orienta-

tion) versus asymmetric input (the stripes seen by each of the two eyes are perpendicular) have not been investigated systematically. In particular, all cylinder experiments have used symmetric binocular input, while goggle experiments have used both types.

In the experiments described in this report we have compared goggle and cylinder rearing under conditions of symmetric and asymmetric binocular input. We reared four groups of animals (i) goggle reared, one eye seeing horizontal and one eye seeing vertical (HV goggle), (ii) goggle reared, both eyes seeing horizontal (HH goggle), (iii) cylinder reared, one eye seeing horizontal, one eye seeing vertical (HV cylinder), and (iv) cylinder reared, both eyes seeing horizontal (HH cylinder).

All animals were put into a dark room at about the time of natural eye opening. At about 3 weeks of age stripe rearing began. For 1 hour per day, the animals wore goggles or were placed in a striped cylinder. All but one of the cats was reared with alternating occlusion. For HV cats this meant that on alternate days one eye was exposed and the animal saw horizontal stripes or the other eye was exposed and the animal saw vertical stripes. One HV goggle animal was reared with simultaneous exposure; one eye saw horizontal stripes at the same time as the other eye saw vertical stripes.

When a cat was used in more than one recording session, it was usually maintained in the dark before the second and subsequent experiments (ten experiments). In six experiments, the animals received daily exposure to the goggles or cylinders between experiments.

Control data were obtained from ani-

mals reared (for a different study) with alternating occlusion but with exposure to a normal repertoire of visual stimuli.

The stimuli in the goggles consisted of black stripes on transparent film. These were mounted in the goggles at the focal point of a lens with a 25-mm focal length so that the stimuli would be focused on the retina without accommodation. Milky plexiglass was placed behind the transparencies so that the stripes appeared to be alternating black and white. Each eye saw a circular visual field, 44° in diameter, and the stripes extended the entire chord of the circle. The widths of the stripes ranged from 0.16° to 3.0°.

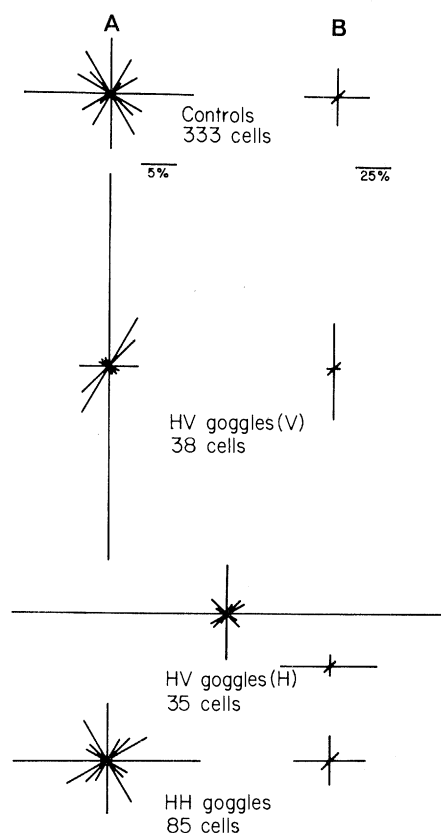


Fig. 1. Orientation preferences of control cats and cats reared viewing striped goggles are diagrammed in two ways. (A) the cells are divided into categories at 30° intervals, except that cells whose preferred orientation had equal horizontal and vertical components are plotted on the 45° and 135° lines. The length of each line is proportional to the proportion of cells preferring stimuli oriented along that line. *HV goggle (V)*, star plot for all HV goggle cells driven exclusively or almost exclusively (groups 1, 2, 6, or 7) by the eye that saw vertical stripes, and *HV goggle (H)*, star plot for those cells driven exclusively or almost exclusively by the eye that saw horizontal stripes. (B) All cells preferring orientations within 30° of vertical have been collapsed along the vertical line, all cells preferring orientations within 30° of horizontal have been collapsed along the horizontal line, and all cells preferring diagonally oriented stimuli have been collapsed along the 45° line.

The cylinders were 522 mm in diameter and 920 mm high and had black and white stripes covering the vertical walls. Since the distance from the kittens' eyes to the cylinders was not constant, the angular size of the stripes cannot be determined precisely, but ranged from about 0.24° to 10°. The kittens sat inside a clear plexiglass cylinder 297 mm in diameter placed inside the striped cylinder. The base of the inner cylinder was 310 mm above the base of the outer cylinder. The kittens wore ruffs to prevent their seeing their own limbs.

We recorded from single units in the visual cortex using conventional extracellular recording techniques (8). We used hand-held stimuli to determine the orientation preference and ocular dominance preference of each cell. There were at least two animals in each group, and we recorded from at least 73 oriented cells in each group. In nine of the experiments, we photographed the cats before and after paralysis in order to measure eye torsion. The difference between pre- and postparalysis angles never exceeded 10.5° inward or 1° outward. In only one case was it greater than 6° inward. Because the cells in deprived animals respond erratically, we were not able to determine preferred orientation with an accuracy greater than 10° to 15°. Therefore, we did not correct for eye torsion in plotting our results.

Figures 1 and 2 present a pictorial representation of the data obtained from animals reared with goggles and cylinders, respectively. The data from the one HV goggle animal reared with simultaneous exposure have been combined with those from the HV goggle animals reared with alternating occlusion. The proportion of orientation-selective cells preferring orientations within 30° of the orientation seen during rearing was almost the same whether or not this animal was included (.70 without the simultaneous animal and .78 with the simultaneous animal included). Similarly, the data for experiments in which the animals lived in the dark between experiments were combined with the data from experiments in which the animals were exposed to the stripes between experiments. The proportion of orientation-selective cells preferring stimuli within 30° of the orientation seen during rearing was virtually identical in both groups (.55 and .56).

The star plots suggest that both of the HV conditions are effective in influencing the distribution of orientation preferences. In both the HV goggle and the HV cylinder conditions most of the cells have preferred orientations within 30° of

the orientation seen during rearing. On the other hand, both HH conditions show little if any effect of the rearing procedure. Thus, asymmetric input is an important factor in the modification of the distribution of orientation selectivity.

To determine whether goggle rearing is more effective than cylinder rearing, one must compare HV goggle cats with HV cylinder cats. (Since neither the HH goggle cats nor the HH cylinder cats show a clear effect of rearing, these two groups cannot be usefully compared.) Figures 1 and 2 show that even though approximately the same percentage of cells falls within 30° of the rearing orientation in the HV goggle and in the HV cylinder cats, the goggles produced a tighter clustering around the experienced orientation.

In order to determine whether the conclusions are statistically reliable, we performed a one-way hierarchical analysis of variance on the data (9). A single data point was obtained from each penetration by calculating the proportion of orientation-selective cells having preferred orientations within 30° of the rearing orientation. For control animals the value assigned to each penetration was the proportion of orientation-selective cells with preferred orientations within 30° of horizontal. Since an analysis of variance requires more than one observation per cell, this analysis excluded two animals for which we had only one

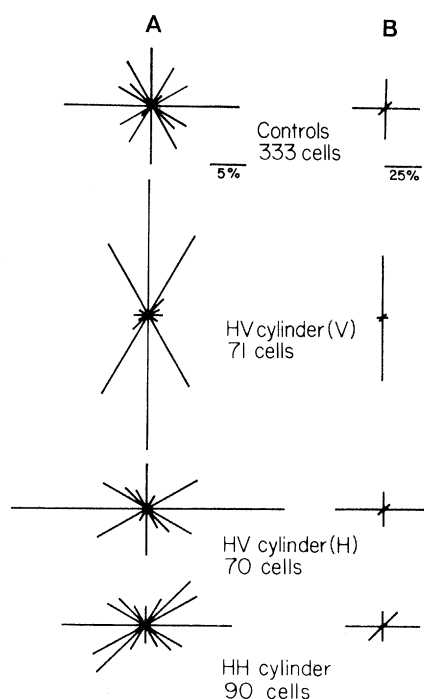


Fig. 2. Orientation preferences of control cats and cats reared viewing striped cylinders. Conventions are as in Fig. 1.

penetration. Pairwise comparisons among group means were made using Fisher's least significant difference (LSD) test (9).

The analysis of variance showed that treatment conditions were effective ($F = 15.3$, $P \leq .02$), and Table 1 indicates which means were significantly different from each other. That both the HV goggle and HV cylinder conditions were significantly different from the controls, whereas the HH conditions were not, allowed us to conclude that asymmetric visual experience is important in controlling the distribution of orientation selectivity. The HV goggle animals did not differ from the HV cylinder animals, indicating that goggles and cylinders are equally effective in reducing the proportion of cells with preferred orientations more than 30° from the rearing orientation. Our method of assigning a value to each penetration did not distinguish between cells whose preferred orientation was the same as the rearing orientation and cells whose orientation was 30° away from the rearing orientation. Therefore, the procedure could not determine whether the goggles produced a tighter clustering around the rearing orientation than the cylinders did.

All four groups of orientation-deprived animals had a large number of abnormal cells. Some were visually unresponsive (from 16 to 27 percent, depending on the group). Some were visually responsive but unoriented (from 18 to 31 percent). Cells classified as unoriented responded equally well or almost equally well to elongated stimuli in all orientations. Five percent of the orientation-selective cells in the HV goggle animals had different orientation preferences through each of the two eyes, or were orientation selective through one eye and nonselective through the other. These abnormal cells were not included in the figures or the data analysis.

A number of possible artifacts in this type of experiment have been discussed by Stryker and Sherk (5), and Stryker *et al.* (7). (i) Experimenter bias cannot be ruled out conclusively, since not all of our experiments were conducted blind, but several facts suggest that experimenter bias did not determine our results. The experiment with one of our early HH cylinder cats was conducted blind, and this cat showed a clear predominance of horizontal preferring cells. When we recorded from an HV animal, we did not know which eye had seen vertical and which horizontal. The HH goggle animals, in which we expected to see a rearing effect, showed none. (ii)

Table 1. Pairwise comparisons of means according to the LSD test: $\alpha = .02$.

Comparison	Difference between means	Significance
HH goggles-controls	.18	$P > .02$
HV goggles-controls	.21	$P \leq .02$
HH cylinders-controls	.03	$P > .02$
HV cylinders-controls	.28	$P \leq .02$
HH cylinders-HH goggles	.15	$P > .02$
HV goggles-HV cylinders	.08	$P > .02$

Stryker and Sherk (5) suggested that bias can result if orientation is not determined by computer, but Blasdel *et al.* (4) have shown that orientation preferences determined by hand plotting agree closely with those determined by computer. (iii) Penetrations perpendicular to the cortex may remain within single orientation and ocular dominance columns, thus biasing the sample. In our experiments each condition included at least two animals and eight penetrations. Furthermore, each penetration went through an average of 4.7 ocular dominance shifts. If a cell is strongly dominated by one eye (groups 1, 2, 6, or 7), an ocular dominance shift is defined as a shift to strong dominance by the other eye or to binocular driving (groups 3, 4, or 5). If a cell is binocularly driven, an ocular dominance shift is a change to strong dominance by one eye. Since ocular dominance columns are larger than orientation columns [the hypercolumns for orientation and ocular dominance are about the same size (10)], it is unlikely that we could go through so many ocular dominance columns while remaining in the same orientation column.

In comparing our results with those of others, we find complete agreement only for the HV goggle condition: all investigators have found a dramatic effect of stripe rearing (6, 7). Both the HH goggle and the HH cylinder conditions have produced conflicting results. Our HH goggle results differ strikingly from those of Stryker *et al.* (7), who found that HH goggles produced almost as good control over orientation selectivity as did HV goggles. One possible explanation for this difference is that Stryker *et al.*'s animals were exposed to the striped goggles for 2 to 5 hours per day, whereas our animals were exposed for only 1 hour per day. Perhaps symmetrical input requires more exposure to produce an effect on

orientation preference. Our HH cylinder data agree with those of Stryker and Sherk, but disagree with those reported by Pettigrew's laboratory (4) and Blake-more's laboratory (2, 3). We cannot compare our HV cylinder results with those of others because the results of this condition have not been previously reported. We conclude that asymmetric input is the most effective way to alter the distribution of orientation preferences of cortical cells. Although symmetric input is effective in some experiments (2-4, 7), it produces much more variable results.

Currently, three mechanisms have been proposed to explain the effect of early experience on the distribution of preferred orientations. (i) Individual neurons may change their orientation preferences in response to restricted early experience. (ii) Cells with preferred orientations inconsistent with rearing may drop out, becoming the unresponsive and unoriented cells. (iii) In the HV animals, cells preferring both the horizontal and the vertical can remain consistent with rearing by maintaining functional connections only with the appropriate eye. The superiority of the HV conditions in altering the distribution of preferred orientations suggests that this mechanism operates. Either or both of the first two mechanisms may also be involved.

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References and Notes

1. D. H. Hubel and T. N. Wiesel, *J. Physiol. (London)* **160**, 106 (1962).
2. C. Blakemore and G. F. Cooper, *Nature (London)* **228**, 477 (1970).
3. C. Blakemore and D. E. Mitchell, *ibid.* **241**, 467 (1973).
4. G. G. Blasdel, D. E. Mitchell, D. W. Muir, J. D. Pettigrew, *J. Physiol. (London)* **265**, 615 (1977).
5. M. P. Stryker and H. Sherk, *Science* **190**, 904 (1975).
6. H. V. B. Hirsch and D. N. Spinelli, *ibid.* **168**, 869 (1970); *Exp. Brain Res.* **12**, 509 (1971); A. G. Leventhal and H. V. B. Hirsch, *Science* **190**, 902 (1975).
7. M. P. Stryker, H. Sherk, A. G. Leventhal, H. V. B. Hirsch, *J. Neurophysiol.* **41**, 896 (1978).
8. B. Gordon and J. Presson, *ibid.* **40**, 1406 (1977).
9. This statistical method was selected to solve two problems. (i) Because individual cells in a penetration are not independent observations, we used summary measures from each penetration as data points. (ii) We wanted to make multiple comparisons among groups, which inflates the significance level unless an analysis of variance shows that the experimental condition exerts a significant effect. The LSD test then allows pairwise comparisons between means [R. E. Kirk, *Experimental Design: Procedures for the Behavioral Sciences* (Brooks/Cole, Belmont, Calif. 1968)].
10. D. H. Hubel, T. N. Wiesel, M. P. Stryker, *J. Comp. Neurol.* **177**, 361 (1978).
11. We thank E. Aamodt for excellent technical assistance. Supported by grant EY 00125 from the National Eye Institute.

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