

biosynthesis and deposition of collagen in rat brain vessels and in testicular arteries as it does in other peripheral large blood vessels. In preliminary studies it has been shown that epinephrine-thyroxine treated rabbits, which exhibit increased collagen synthesis in peripheral blood vessels (7), also show increases in prolyl hydroxylase and in the in vitro synthesis of collagen in brain microvessels.

Pathologic examination of the rats showed that after 6 weeks of treatment with DOCA-salt, there was only occasional and mild fibrinoid necrosis in arteries and arterioles of the brain, pial membrane, and testes, which correspond to the changes observed by Gardner and Matthews (11). The large artery (aorta) and arteries of medium caliber (basilar artery, mesenteric artery, and circle of Willis) showed no pathological changes except for a slight thickening of the vascular wall.

The findings reported here indicate that there is increased collagen biosynthesis in arterioles and arteries in the periphery and in the central nervous system of DOCA-salt hypertensive rats and provide an early biochemical indication that fibrogenesis is involved in the production of hypertensive vascular damage (arteriosclerosis). It was previously shown (1) that the increase in prolyl hydroxylase activity is the result of increased production of the enzyme. We have calculated that DOCA-salt treatment increases synthesis of vascular collagen and prolyl hydroxylase to a far greater extent than it does total protein. These observations lend further biochemical support to the findings of Freis and co-workers (12) and of Hollander (13) that hypertension shortens life and produces pathologic lesions and that these changes are prevented by antihypertensive drugs. It is also likely that the structural hypertrophy of the resistance vessels induced by hypertension (14) is, at least in part, due to collagen deposition. As far as the brain microvessels are concerned, it is interesting to consider the possibility that in untreated hypertension, deposition of small amounts of collagen, in quantities insufficient to be observed by standard pathologic techniques as frank arteriosclerosis, could nevertheless alter vascular permeability and transport mechanisms and thereby diminish mental function.

A. OOSHIMA

Roche Institute of Molecular Biology,
Nutley, New Jersey 07110

G. FULLER

University of Rhode Island,
Kingston 02881

G. CARDINALE

S. SPECTOR

S. UDENFRIEND

Roche Institute of Molecular Biology

References and Notes

1. A. Ooshima, G. C. Fuller, G. J. Cardinale, S. Spector, S. Udenfriend, *Proc. Natl. Acad. Sci. U.S.A.* **71**, 3019 (1974).
2. K. Brendel, E. Meezan, E. C. Carlson, *Science* **185**, 953 (1974).
3. J. DeChamplain, L. R. Krakoff, J. Axelrod, *Circ. Res.* **23**, 479 (1968); J. DeChamplain and M. R. van Ameringen, *ibid.* **31**, 617 (1972).
4. J. R. Williams, T. R. Harrison, A. Grollman, *J. Clin. Invest.* **18**, 373 (1939).
5. *N*-2-Hydroxyethylpiperazine-*N*-2-ethanesulfonic acid.
6. J. J. Hutton, Jr., A. L. Tappel, S. Udenfriend, *Anal. Biochem.* **16**, 384 (1966).
7. G. C. Fuller and R. O. Langer, *Science* **168**, 987 (1970).
8. O. H. Lowry, N. J. Rosebrough, A. L. Farr, R. J. Randall, *J. Biol. Chem.* **193**, 265 (1951).
9. K. Burton, *Biochem. J.* **62**, 315 (1956).
10. Reserpine, in the doses given here, also lowers prolyl hydroxylase in tissues other than blood vessels, as might be expected from its effect on rat growth (Table 1). However, reserpine lowers vascular prolyl hydroxylase far more than it does prolyl hydroxylase in other tissues. Both chlorothiazide and reserpine were found to reverse the effects of hypertension on vascular collagen synthesis (1). It was noted that the response treated animals yielded values that were even lower than the normotensive controls, indicating that this drug has an effect over and above its effect on blood pressure.
11. D. L. Gardner and M. A. Matthews, *J. Pathol.* **97**, 51 (1969).
12. E. D. Freis, D. Ragan, H. Pillsbury, III, M. Matthews, *Circ. Res.* **31**, 1 (1972); E. D. Freis, *Circ. Res. Suppl.* **2** **29**, 70 (1971).
13. W. Hollander, *Circulation* **48**, 1112 (1973).
14. B. Folkow, M. Hallback, Y. Lundgren, R. Sivertsson, L. Weiss, *Circ. Res. Suppl.* **1** **32**, 33, 2 (1973).

23 June 1975; revised 13 August 1975

Oriental Anisotropy in Infant Vision

Abstract. *Infants prefer to look at horizontal and vertical gratings rather than at oblique gratings only when they are at or near threshold spatial frequencies, as would be expected if acuity for oblique edges is lower than that for horizontal and vertical edges. That such a bias exists as early as 6 weeks of age suggests that the orientational asymmetry of the visual system depends on endogenous maturation rather than exposure to a carpentered world.*

Under a wide variety of conditions, the visual acuity of adult human observers is greater for horizontal and vertical edges than for oblique edges (1, 2). This "oblique effect" has been attributed to early visual experience in our carpentered environment, with its preponderance of vertical and horizontal contours (3). The notion that the sensitivity of the visual system to contours of various orientations is shaped at an early stage of development by the prevalence and clarity of the edges to which the eye is exposed implies a form of

neural plasticity. This viewpoint is supported by claims that the distribution of orientation-sensitive single units in the visual cortices of kittens is altered by rearing the kittens in orientationally biased environments (4) and by reports that astigmatic human observers suffer a residual loss of acuity for edges along the blurred axis even when optical factors are eliminated (5).

If environmental exposure were responsible for the orientational asymmetries in the visual system, then these asymmetries should not be evident prior to an appropriate period of exposure. Evidence for an oblique effect has been described in 2-year-old children (6), but in the only study of infant acuity as a function of edge orientation, no meridional differences in sensitivity were observed (7). However, using a similar but more sensitive technique, we have found that the oblique effect is present in human infants as young as 6 weeks of age. Our result casts doubt upon explanations of the oblique effect solely in terms of environmental biasing.

We investigated the development of orientational differences in the acuity of infants using a modification of Teller *et al.*'s two-alternative preferential looking technique (7). It has been demonstrated that infants preferentially fixate patterned over homogeneous stimuli (8). Teller *et al.* paired a grating of a given orientation with a homogeneous gray target of equal luminance. We simultaneously presented two gratings of the same spatial frequency (one cycle consists of one bar and one space of equal width) but of different orientations. Our technique is based on the premise that an infant will preferentially fixate the more

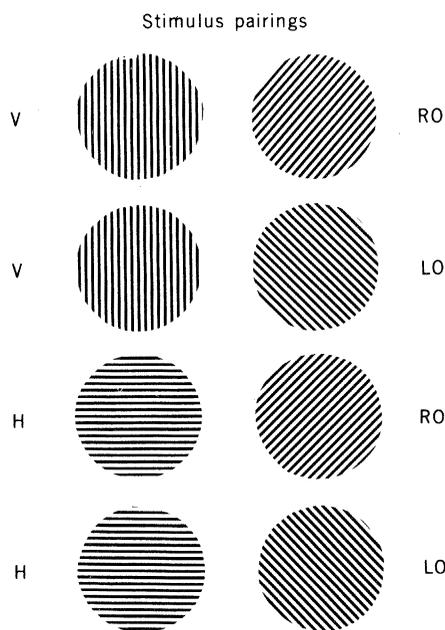


Fig. 1. Schematic representation of stimulus pairs. In all cases, either a vertical or a horizontal grating was paired with a left- or a right-oblique grating of the same spatial frequency.

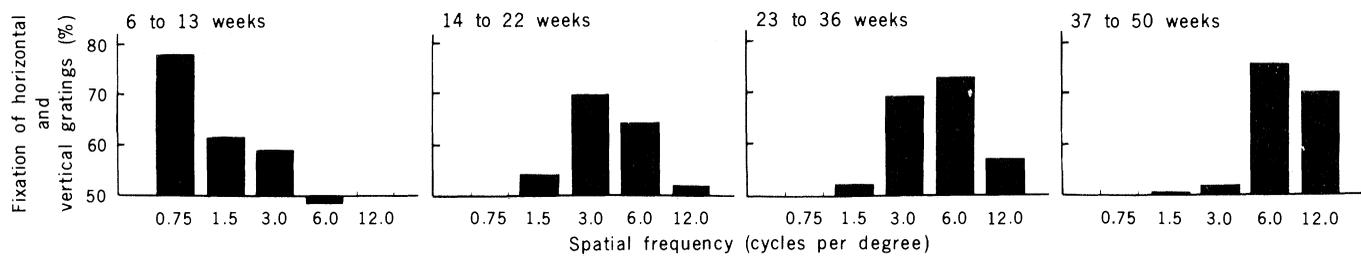


Fig. 2. Mean percentage of vertical and horizontal gratings looked at for the four age groups. Data for spatial frequencies of 0.75, 1.5, 3.0, and 6.0 cycles per degree are given for the youngest group and for spatial frequencies of 1.5, 3.0, 6.0, and 12.0 cycles per degree for the three older groups.

clearly visible of two simultaneously presented target gratings. At a given spatial frequency, a vertical (or horizontal) and an oblique grating may both be visible, and therefore both be preferentially fixated over a gray target; but one of the orientations may, in fact, appear clearer than the other. While such a difference in orientational visibility could go undetected by the pattern versus gray technique, the pattern versus pattern technique might detect the difference.

Full-term infants ranging from 6 to 50 weeks of age were tested. Each infant was refracted by retinoscopy, and only infants showing no appreciable astigmatism were included in the sample (9). Subjects were placed in one of four age groups (6 to 13 weeks, 14 to 22 weeks, 23 to 36 weeks, and 37 to 50 weeks); there were six infants in each group.

The apparatus consisted of a wooden partition with two circular screens, one to the right and one to the left of a fixation light; each subtended 11° of visual angle, and they were separated by 25° of visual angle. Black and white square wave gratings of 93 percent contrast (10) were projected onto the rear of the screens to yield a mean luminance of 34 cd/m^2 . Stimuli consisted of four orientations (0° , 45° , 90° , and 135°) at five frequencies (0.75, 1.5, 3.0, 6.0, and 12.0 cycles per degree of visual angle) (11). On each trial, a vertical or horizontal grating was presented with a left- or right-oblique grating of the same spatial frequency for 10 seconds. The four combinations are shown in Fig. 1. Side of presentation was counterbalanced for both frequency and orientation, and the order of presentation of stimulus pairs was randomized. In most cases, 48 trials were run per session (12).

During an experimental session, the infant either sat on the parent's lap or was held over the parent's shoulder (13). Before each trial, the infant's head was centered with respect to the two targets and the fixation light was flashed in order to realign his gaze. Viewing distance was $52 \pm 3 \text{ cm}$ from each target (14). During each trial, an observer looked at the infant's head and eye movements through a peephole and made a forced-choice judgment as to which

side the infant preferentially fixated. The observer neither saw the paired gratings nor knew the sequence of the stimuli.

The results showed no significant differences in the preferences (t -test, $d.f. = 5$, $P > .10$) between verticals and horizontals or right-obliques and left-obliques at any of the spatial frequencies tested for each age group. Consequently, we combined the data for verticals and horizontals and the data for the two oblique orientations. Figure 2 shows the percentage of total trials on which vertical and horizontal gratings were fixated for each spatial frequency tested for the four age groups. In a two-alternative forced-choice technique subjects would be expected to look at verticals and horizontals 50 percent of the time and at obliques the other 50 percent of the time by chance. An analysis of variance revealed a significant interaction among age, spatial frequency, and orientation ($F = 1.926$; $d.f. = 18,135$; $P < .01$). The youngest age group (6 to 13 weeks) showed a maximum preference for verticals and horizontals over obliques at the lowest frequency tested (0.75 cycle per degree). The 14- to 22-week age group showed a peak preference at 3.0 cycles per degree, while the 23- to 36-week group peaked at 6.0 cycles per degree. For the oldest group (37 to 50 weeks), the peak preference for vertical and horizontal patterns over oblique ones lay between 6.0 and 12.0 cycles per degree. This peak shift closely follows the shift in infant acuity with age previously obtained by the technique of preferential looking (7, 8). We believe that the maximum difference in the frequency of looking at the various orientations occurs at the threshold spatial frequency for each age group, presumably because horizontal and vertical gratings are more clearly visible than otherwise equivalent oblique gratings (15, 16).

The choice of horizontal and vertical gratings declines at both high and low frequencies. We conclude that, at high frequencies, the falloff indicates decreasing ability to resolve either grating (both are below threshold) and, at low frequencies, the falloff indicates increasing ability to resolve both gratings (both are well above threshold and visibility differences are

minimal). An explanation of the data in terms of a conceptually based preference is precluded by the equalization of orientational choices at spatial frequencies well above threshold. The infants do not simply prefer looking at horizontal and vertical gratings to looking at oblique gratings.

In summary, our results indicate the existence of an oblique effect as early as 6 weeks of age. It is unlikely that during the first 6 weeks of life, the infants' retinas are exposed to more vertical and horizontal than oblique edges, since such young infants spend much of their waking time in prone or supine positions. Thus, the occurrence of an oblique effect by 6 weeks of age argues against an interpretation of this form of meridional anisotropy as resulting solely from prolonged exposure to an asymmetrical distribution of edges on the retina.

SUSAN COHEN LEEHEY

ANNE MOSKOWITZ-COOK

SARAH BRILL, RICHARD HELD

Department of Psychology,

Massachusetts Institute of Technology,

Cambridge 02139

References and Notes

1. For a review of these findings, see S. Appelle, *Psychol. Bull.* **78**, 226 (1972).
2. The oblique effect cannot be accounted for wholly in terms of optical astigmatism [H. Leibowitz, *J. Opt. Soc. Am.* **43**, 902 (1953); F. W. Campbell, J. J. Kulikowski, J. Levinson, *J. Physiol. (Lond.)* **187**, 427 (1966); D. E. Mitchell, R. D. Freeman, G. Westheimer, *J. Opt. Soc. Am.* **57**, 246 (1967)], eye movements [G. C. Higgins and K. A. Stultz, *ibid.* **40**, 135 (1950); J. Nachmias, *ibid.* **50**, 569 (1960)], or variations in receptor density [S. L. Polyak, *The Retina* (Univ. of Chicago Press, Chicago, 1941)]. The electroretinogram does not exhibit the oblique effect, which indicates that the effect is mediated by neural structures more central than the site of the electroretinogram [L. Maffei and F. W. Campbell, *Science* **167**, 386 (1970)].
3. R. C. Annis and B. Frost, *Science* **182**, 729 (1973).
4. C. Blakemore and G. F. Cooper, *Nature (Lond.)* **228**, 477 (1970); H. V. B. Hirsch and D. N. Spinelli, *Science* **168**, 869 (1970); C. Blakemore and D. E. Mitchell, *Nature (Lond.)* **241**, 467 (1973); R. D. Freeman and J. D. Pettigrew, *ibid.* **246**, 359 (1973); C. Blakemore, in *The Neurosciences, Third Study Program*, F. G. Worden and F. O. Schmitt, Eds. (MIT Press, Cambridge, Mass., 1974), p. 105. But see M. P. Stryker and H. Sherk, *Science* **190**, 904 (1975).
5. R. D. Freeman, D. E. Mitchell, M. Millodot, *Science* **175**, 1384 (1972); D. E. Mitchell, R. D. Freeman, M. Millodot, G. Haegerstrom, *Vision Res.* **13**, 535 (1973); R. D. Freeman and L. N. Thibos, *Science* **180**, 876 (1973); A. Fiorentini and L. Maffei, *Vision Res.* **13**, 1781 (1973).
6. F. C. Volkman and D. C. Prizer, paper presented at the Eastern Psychological Association Convention, Washington, D.C., May 1973.
7. D. Teller, R. Morse, R. Borton, D. Regal, *Vision Res.* **14**, 1433 (1974).

8. R. Fantz, J. Ordy, M. Udelf, *J. Comp. Physiol. Psychol.* **55**, 907 (1955).
9. Detection of spherical refractive error by retinoscopy is made difficult by uncontrolled variations in the accommodative state of the infant's eye. However, since spherical error would equally effect the response to targets of all orientations, such defects cannot account for relative orientational differences. We thank Dr. S. Wittenberg and Dr. I. Mohindra, Massachusetts College of Optometry, for performing the retinoscopy.
10. Contrast was calculated from the following formula: $(L_1 - L_2)/(L_1 + L_2)$, where L_1 is the luminance of the light area and L_2 the luminance of the dark area.
11. In accordance with previously determined differences in acuity as a function of age (7, 8), the youngest group was tested with gratings of 0.75, 1.5, 3.0, and 6.0 cycle/degree, while 1.5, 3.0, 6.0, and 12.0 cycle/degree gratings were used for the older age groups.
12. Two experimental sessions were run on most subjects. Approximately 64 trials were obtained on each subject in the youngest age group (6 to 13 weeks), and approximately 109 trials for each subject in the three older groups (14 to 22 weeks, 23 to 36 weeks, and 37 to 50 weeks). For infants in the youngest group, we often obtained fewer than 48 trials per session because of lack of subject cooperation.
13. There were no appreciable differences between results obtained with the parents facing toward or away from the stimulus targets; this makes it unlikely that the parents were biasing the infant's looking behavior. Furthermore, the possibility that the few parents who had any knowledge of the oblique effect could have predicted its interaction with spatial frequency is slight.
14. By 2 months of age, the infant's accommodative capacity is sufficiently developed to allow sharp focusing of targets at this distance [H. Haynes, B. L. White, R. Held, *Science* **148**, 528 (1965)].
15. Subjects showed an elevated fixation percentage for vertical and horizontal patterns at more than one spatial frequency. This dispersion in the data can be explained either if the actual threshold for subjects in a given age group lies between two of the spatial frequencies tested or if subjects in a given group have slightly different thresholds, or both.
16. The possibility exists that instead of measuring the infant's limit of resolution (his threshold), the preferential looking technique is a measure of the spatial frequency beyond which the infant no longer attends to visual stimuli. But, even if this were the case, our finding of differential responses to vertical and horizontal versus oblique gratings would imply an underlying disparity in orientational visibility.
17. Supported by NIH grant ROI EY01191, NASA grant NGL 22-009-308, and the Spencer Foundation.

17 April 1975

Cortical Effect of Early Selective Exposure to Diagonal Lines

Abstract. *Neurons in the visual cortex that respond preferentially to diagonal contours are present only in cats exposed to diagonal lines early in life. In contrast, cells that prefer horizontal or vertical contours are found following exposure to horizontal, to vertical, and to diagonal lines. Such cells do not require a specific visual input for maintenance or for development; neurons responding preferentially to diagonal lines do.*

Most neurons in the visual cortex of the cat and the monkey respond maximally to line-shaped stimuli presented at a given orientation and position on the retina (1). The particular stimulus orientation that elicits a maximum response varies from cell to cell. If an animal's early postnatal visual experience is restricted, the distribution of these neurons, and to some extent the animal's behavioral capabilities, are modified (2, 3). The precise conditions necessary for the development of orientation specificity, however, remain unclear (4, 5).

In a wide range of animals, including man, behavioral and physiological evidence indicates that the visual system responds preferentially to horizontal and vertical patterns (6). To determine whether this bias is a consequence of an animal's early visual experience, we compared the effects of early selective exposure to diagonal lines and to horizontal and vertical lines. In cats exposed only to horizontal and vertical patterns, nearly all orientation-sensitive cells studied responded most strongly to lines oriented either horizontally or vertically (2). In contrast, in cats exposed to diagonal patterns alone, we found more cortical cells responding preferentially to horizontal or to vertical lines than to diagonal patterns. Since, with our techniques, the cat's visual system cannot be made to respond preferentially to diagonal

lines, we suggest that the preferential response of the visual system to horizontal and to vertical lines reflects its inherent organization and is not simply the response to an early visual environment dominated by horizontal and vertical contours.

Eight cats born in a laboratory colony served as experimental subjects. They were housed with their mother in total darkness from birth. Beginning at 4 weeks of age the animals were exposed daily to a controlled visual environment; they were fitted with masks within which each eye could view a circular field, 40° to 50° in diameter, containing three parallel black lines on a white background (2). The lines were 1° wide, their centers separated by 6°, and their ends blurred and distorted by the lenses. At the end of an 8-hour exposure period the animals were returned to their mother. Since the masks were put on and taken off in the darkroom, the animals' only visual experiences were provided by the masks.

Three cats viewed vertical stripes with one eye and, simultaneously, horizontal stripes with the other eye. Five other animals viewed a similar pattern, but the stripes were oriented at 45° for one eye and at 135° for the other.

Selective exposure was continued daily until the animals had been exposed to the patterns for approximately 100 hours. Subsequently, all of the animals remained

in the darkroom until they were at least 16 weeks of age (7). Four cats were then exposed for 6 months to a normally illuminated environment before single unit recordings were made. Two cats had both eyes sutured shut immediately after they were removed from the darkroom, and two were left in the darkroom until the recordings were carried out. These four animals thus received no patterned visual stimulation subsequent to the selective exposure provided during the rearing. Three cats raised from birth in a normally illuminated laboratory colony served as control animals.

The response properties of single units in the visual cortex were determined with conventional procedures (1, 5, 8). Animals were anesthetized with either Fluothane or Sodium Pentothal during preparation for recording. The skin, bone, and dura over the striate cortex were removed, and a chamber was positioned over this craniotomy. The animals were paralyzed with intravenously infused *d*-tubocurarine and gallamine triethiodide (Flaxedil) and artificially ventilated with a mixture of nitrous oxide, oxygen, and carbon dioxide. Incisions and pressure points were infiltrated with a long-acting local anesthetic, and general anesthesia was discontinued. Standard procedures were used to protect the eyes, correct the optics, and minimize eye movements. The projections of the optic disc were plotted and the position of the area centralis inferred (9). Recording began after the animal had recovered from general anesthesia.

An Insl-x-coated tungsten microelectrode was lowered hydraulically through the medial bank of the primary visual cortex (5, 10, 11), and responses of single units were amplified and isolated. Once a unit had been isolated, ocular dominance was determined (1). Line-shaped stimuli were presented with a hand-held projector in order to test the cell's response properties. Minimum response fields were obtained for each unit (8), and directional selectivity was assessed (12). For units showing orientation-sensitivity, the preferred orientation and the range of orientations that activate the cell were determined (11).

Data were collected from 210 units in experimental animals and from 50 units in normal cats. The receptive fields of most cells were within 15° of the estimated projection of the area centralis. In normal animals, units were activated binocularly (92 percent) and displayed a full range of orientation preferences as reported by others (1, 8, 13).

The distribution of the preferred orientations of units examined in the three animals exposed to vertical stripes with the