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abnormal responses from the eye with reduced acuity. The four patients with optic atrophy showed normal ERGs (amplitudes 0.18 to 0.34µV; implicit times 36 to 37 msec).

Discussion
Foveal cone ERGs recorded from the ambiopic eyes of fifteen patients with strabismic amblyopia were normal in amplitude and b-wave implicit time. Moreover, the differences in ERGs between the amblyopic and the normal fellow eyes were no greater than those observed between the left and right eyes of fifteen normal subjects of comparable age. The typical decrease in amplitude of the foveal cone ERG that occurs with eccentricity from the fovea in normal eyes, consistent with the known decrease in cone density in the parafovea compared with the fovea (Osterberg, 1935), was also present in amblyopic eyes.

Previous investigations that have reported abnormalities in the ERG of patients with amblyopia must be interpreted with caution. In his review of ERG studies in amblyopia, Burian (1967) disagreed most of the reported abnormalities on technical or theoretical grounds. Even in recent ERG studies using patterned stimuli (Tuttle, 1972; Sekol and Nadler, 1979), it has not been certain that the stimulus was in focus and maintained on the amblyopic fovea throughout testing. With the stimulator-ocephalothoracic problems have been reduced to a minimum. The foveal nature of our stimulus was substantiated by the fact that patients with macular scars of one disc diameter gave undetectable responses. The technique proved sensitive for detection of foveal pre-ganglion cell retinal abnormalities in patients with juvenile hereditary macular degeneration and visual acuity of 6/15 or below (Sandberg and others, 1979). The cone specificity of the stimulus was confirmed when undetectable responses were obtained in recordings from a rod monochromat (Sandberg and others, 1979) and in the observation that decreasing ERG amplitude occurs with increasing eccentricity from the fovea.

The possibility exists that a test of even greater sensitivity that is used in the present investigation, such as a foveal cone ERG elicited with a stimulus smaller than 4°, could reveal a functional abnormality in the retina. The size of the stimulus was dictated by the fact that stimuli of smaller diameter yielded less reproducible responses with the current procedure. The adequacy of the stimulus, however, is supported by previous psychophysical estimates of the diameter of the ambiopic scotoma; e.g. 'diameter of the scotoma varies between 2 and 15° (mean 4.7±)' (Duke-Elder and Wybar, 1973). In addition, a recent unicoicotometric study of patients with strabismic amblyopia (many from the present study), using the stimulater-ophthalmoscope and stimuli of 6° to 1° in diameter (Jacobson and Sandberg, in preparation), showed elevated cone increment thresholds not only in the ambiopic fovea but also at parafoveal retinal loci (i.e. 10° nasal to the fovea).

The findings in the present study are consistent with the idea that pre-ganglion cell foveal cone function is normal in human strabismic amblyopia. Whether dysfunc-

tion exists at the retinal ganglion cell level in human strabismic amblyopia as suggested by the work of Ikeda and Tremain (1978) on experimental strabismic amblyopia in cats cannot be decided from the present investigation since the human ERG is known not to be a measure of retinal ganglion cell function (Berson, 1975).

The normal foveal cone ERGs in our patients with optic atrophy serve to re-emphasize this point. In conclusion, the site of the lesion in human amblyopia remains unknown, but the results of the present study weigh against the possibility of a readily detectable physiologi-

cal abnormality in the central retina distal to the ganglion cell layer.

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Functional development of geniculocortical pathways in normal and amblyopic vision

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Summary
The geniculocortical pathways of many mammals, including primates, are largely comprised of two neuron types. These are known as X and Y cells. Their functional significance is unclear, but the following highly speculative hypothesis is suggested. Y cells, because of their broad sensitivity to the visual input, would be involved in a basic analysis of form vision. X cells, because of their fairly selective sensitivity to higher spatial frequencies, add to this certain details (i.e. enhanced acuity, etc.). If an animal develops with ametropia, Y cells should be adequately stimulated and the lower spatial frequencies remain undistorted. Many Y cells would develop and reasonable form vision with mild amblyopia would result. Only X cells would be greatly affected by such an environment. However, if the animal develops with cataracts or is reared in an environment which abolishes all spatial frequencies, then neither X nor Y cells will develop. This would result in poor form vision and a deep amblyopia. Many of these phenomena have been observed in experimental studies of cats. The present relevance of the suggested functional dichotomy for X and Y cells is at best tenuous, and it is offered merely as a working hypothesis for future studies.

The current interest in the central visual pathways of animals raised with visual deprivation can be traced back to the already classic work of Wiesel and Hubel who were the first to demonstrate the functional development of cats raised with one eye sutured shut (Wiesel and Hubel, 1963). This interest is directed not only at basic problems of neural development and plasticity but also at gaining insights into clinical problems, such as amblyopia, by studying appropriate animal models. The significance of these studies for clinical problems should certainly be questioned, particularly since cats are not humans and otherwise normal children rarely have one eye occluded (or any of the variety of artificial rearing conditions to which we subject animals). Nevertheless, such animal studies can provide insights into the types of developmental processes which are susceptible to environmental manipulation.

This thesis could be supported by consideration of any of dozens of research efforts in this area, but to achieve focus and brevity, the remainder of the paper will be limited to studies of geniculocortical cells in cats reared from birth with monocular suture. It is no coincidence that this happens to be the subject upon which our laboratory has focused. No attempt will be made to cover unpublished research involving deprivation regimens other than lid suture, neural areas other than the geniculocortical pathways, or research animals other than cats. The reader is referred instead to recent reviews (Blakemore, 1978; Hirch and Levinthal, 1978).

The geniculocortical pathways of the cat
One reason to study the cat's geniculocortical system is its basic similarity to that of man. Fig. 1 illustrates the wiring diagram for this system, and it can effectively be divided into X and Y pathways.1 Retinal X and Y cells are functionally quite like their geniculate counterparts, but X and Y cells differ from each other in a number of important physiological and anatomical dimensions (see below and Stone and Dreher, 1973; Rowe and Stone, 1976; LeVay and Ferster, 1977; Rodieck, 1979; Friedlander, Liu, and Sherman, 1979). The functional significance of this division into X and Y components remains unclear, and consequently we must substitute speculation for understanding. Since lid suture

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1 A third system, involving W cells, also exists and is related via the most ventral C complex of laminae (see Fig. 1 and Wilson, Rowe, and Stone, 1976; see also Rowe and Stone, and Rodieck, 1976; Rodieck, 1979). This appears to reflect a relatively minor contribution to cortical innervation, but in fact little is known about this pathway in normal cats and nothing is known about the effects of visual deprivation upon W cell development.
affects the X and Y pathways in cats quite differently, and because these effects probably underlie the amblyopia suffered by these cats, it is worth speculating about the role normally played by X and Y cells. The most common suggestion stems from the observations that, compared to Y cells, X cells tend to have smaller receptive fields, display fewer linear or spatial summation, respond better to stationary targets, and are more concentrated in the central representation of the visual field. From these differences, some authors (e.g., Heds and Wright, 1972, 1975) have suggested that X cells analyze spatial patterns leaving an analysis of temporal features and/or movements to Y cells.

More recent studies in several laboratories, including our own, have suggested a different and more complicated interpretation. Our visual world is a rich one composed of a variety of spatial and temporal patterns. The range of these features is typically large. That is, spatial patterns range from very coarse, large objects to fine details; similarly, temporal changes in our world vary from slow movements or changes in brightness to very fast ones. A more precise way to describe these patterns is in terms of spatial and temporal frequencies. Low spatial frequencies are coarse patterns, high frequencies are fine patterns; similarly, low temporal frequencies represent slow changes in the visual scene, while high frequencies represent fast changes. Recently, psychophysicists have begun to analyze vision by measuring sensitivity to stimuli comprised of single spatial and temporal frequencies. This is accomplished by using stimuli in which Y cells are slightly more sensitive than are X cells to higher spatial frequencies, but at lower frequencies Y cells are responsive whereas X cells are relatively unresponsive. The difference in the temporal sensitivity of the two classes represents the major differences between X and Y cell responses to spatiotemporal stimulation (Lehmkuhle and others, 1978).

For many years the importance to vision of low spatial frequencies, which would activate Y cells but not X cells, has been overlooked. Perhaps this is because the most common clinical assessment of visual capacity is an acuity test which measures sensitivity only to the highest spatial frequencies seen. Recent psychophysical work (Krauskopf, Day, and Radley, 1970; Hess and Wool, 1978) has emphasized the importance of the lower spatial frequencies. These studies, in fact, suggest that basic form vision travels in the lower spatial frequencies, and that the higher ones are used to analyse fine detail. Most of us have had experience which supports this conclusion. Blurring of an image (by a poorly focused camera, misted spectacles, etc.) fairly selectively blocks transmission or reduces contrast of higher spatial frequencies with little effect upon lower ones.

Recently, Goldstein (1973) and others have demonstrated that, in a moderately defocussed image, blurring of an image (by dirty spectacles, heavy fog, viewing through waxed paper, etc.) depresses responses to all spatial frequencies roughly equally. If such diffusions reduce transmission of local spatial frequencies sufficiently, spatial vision is severely hampered. In fact, if the same visual scene is distorted by blurring or diffusion so that higher spatial frequencies are more affected by the former than by the latter, that scene typically is much more read no matter how accurate and standard (Hess and Wool, 1978). Again, this emphasizes the importance of low spatial frequencies to form vision.

It is now possible to offer an hypothesis regarding the functional role of X and Y pathways, an hypothesis which differs from the common one based on a spatial and temporal distinction. It seems clear that spatial and temporal frequencies are at least equally important for good form vision. Generally, Y cells seem responsive to these frequencies while X cells are not. Perhaps Y cells cannot, or do not, respond to spatial patterns, but X cells are involved in adding important details to this, such as higher acuity, stereopsis, colour vision, etc. (for a detailed discussion of this see Lehmkuhle and others, 1978).
Sherman, 1978), although the detailed relationship between the physiology and anatomy of this defect is as yet unclear. X cells in deprived laminae are not completely normal, but have a subtle defect (Lehmkuhle, Kritz, Mangel, and Sherman, 1980b). Although responsive to middle spatial frequencies with fairly normal spatial response organization, they are relatively insensitive to higher spatial frequencies. That is, they suffer an acute loss although they retain normal responsiveness to middle spatial frequencies.

Developmental mechanisms of X and Y cells

Another difference between deprivation induced defects in X and Y cells provides important clues for understanding the mechanisms which control their development. This difference lies in the pattern of the above-mentioned abnormalities (see Fig. 2). The loss of recordable geniculate Y cells is limited to the deprived binocular segment of the nucleus, whereas the deprived monocular segment has normal laminae and numbers (Sherman and others, 1972; Lehmkuhle and others, 1980b). The acute loss for geniculate X cells, on the other hand, is seen throughout the nucleus, and is roughly equal in magnitude in the deprived and normal segments.

The binocular segment of the central visual pathways, including the lateral geniculate nucleus, is that portion in which the neurons have receptive fields within the binocularly viewed portion of the visual field. The monocular segments contain neurons of which the receptive fields are in the monocularly viewed portion of the visual field. The cat's visual field horizontally spans roughly 180°. The central 90° is the binocular segment and the peripheral 45° on each side is the monocular segment (see Sherman, Hoffmann, and Stone, 1972; Sherman, Gtiolley, Kaas, and Sanderson, 1974).

The deprived geniculate Y cells are located anywhere in the deprived binocular segment, but the deprived monocular segment contains these cells in normal numbers.
Development of the neural basis of visual acuity in monkeys

Speculation on the origin of deprivation amblyopia

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The effects on the developing visual cortex of even brief periods of unioocular deprivation in kittens and baby monkeys (Wiesel and Hubel, 1965; Hubel and Wiesel, 1970; Crawford, Blake, Cool, and von Noorden, 1975; Hubel, Wiesel, and Le Vay, 1977; Blakemore, Garey, and Vital-Durand, 1978) provide an appealing model for the profound amblyopia that follows early occlusion of one eye in human infants (von Noorden, 1973; Aways, Miyake, Imazumi, Shiote, Kanda, and Komuro, 1973). Cortical neurons, the majority of which are normally responsive to visual stimulation of either eye, rapidly lose their functional input from the deprived eye. This phenomenon has been interpreted in terms of some kind of competitive interaction between inputs from the two eyes at the level of the striate cortex, where the two pathways converge for the first time in the retinogeniculocortical system.

There are a number of delightfully simple analogies to be drawn between the changes in ocular dominance of cortical neurons and the changes of acuity in amblyopic eyes. For instance, in a kitten or baby monkey rendered amblyopic by unioocular deprivation, the ocular dominance of cortical cells can be shifted back in favor of the initially deprived eye by a subsequent period of reverse-suturing—opening the deprived eye and closing the other (Blakemore and Van Sluyters 1974; Blakemore and others, 1978), just as alternate closure of first one eye and then the other in babies leaves amblyopic the eye that is closed second (Aways and others, 1973).

But are things as simple as they seem? Blakemore and Eggers (1978) have pointed out that it is naive to argue from population shifts in the ocular dominance of neurons to relative acuity in the two eyes: as long as an animal has even a tiny fraction of all cortical cells still responsive through its deprived eye it might in principle have quite normal vision through that eye. It is surely the performance of visual neurons, not their mere number, that determines an animal's acuity.

More important, the suggestion has been made, at least for strabismic amblyopia, that subtle changes in neuronal properties earlier in the visual pathway than the cortex itself might explain the reduction in acuity that characterizes amblyopia (see Ikeda, 1979). Ikeda and her colleagues (who first emphasized the importance of testing the role of power of neural network in any attempt to analyse the neural basis of amblyopia) have found that the surgical induction of paralytic esotropia in kittens retards the normal process by which retinal ganglion cells (Ikeda and Tremain, 1979) and neurons of the lateral geniculate nucleus (Ikeda and Wright, 1976) gradually improve their spatial resolving power during the first 2 or 3 months of life. Thus strabismic amblyopia may be essentially a peripheral deficit. Could the same be true for occlusion amblyopia?

Maffei and Fiorentini (1976) and Lehmkuhle, Kratz, Mangel, and Sherman (1978) have indeed reported that unioocular deprivation in kittens leads to an inability of Cells of the lateral geniculate nucleus (LGN) to respond to grating patterns of high spatial frequency presented to the deprived eye. Interestingly, however, the spatial resolving power of retinal ganglion cells in the deprived eye is not affected (Kratz, Mangel, Lehmkuhle, and Sherman, 1979).

We, in this study, have examined this question for the first time in monkeys—a species of much higher visual acuity than the cat, in which the effects of visual deprivation on the development of acuity might therefore be expected to be even more severe. We have recorded from cells in the LGN of monkeys, from the day of birth onwards, and have examined their ability to resolve fine spatial detail. The results show that the normal improvement in neuronal 'acuity' parallels the monkey's actual behavioural visual development, but that, surprisingly, unioocular deprivation has little or no effect on this process.