What Causes Nearsightedness?

Long the subject of debate on the "genes versus environment" theme, an animal model now shows that at least some myopia may be acquired

Twenty-five percent of the American population is estimated to be nearsighted, and no one knows why. In fact, until recently, there were no good ways to study myopia. The investigations have been hampered by lack of a good animal model in which the causes of this disorder could be elucidated so that preventive measures could be developed. But recently, Elio Raviola, of Harvard Medical School, and Torsten Wiesel, who is now at Rockefeller University, have discovered an animal model of myopia that strikingly resembles the human condition. Their results so far indicate that myopia may be caused by abnormal influences of the nervous system on the developing eye.

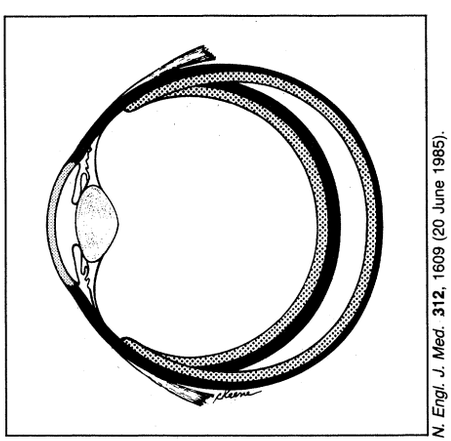
Ophthalmologists have been divided on the causes of myopia. Some argue that it is almost entirely genetically determined—if you inherit a tendency to become nearsighted, your distance vision will gradually deteriorate, starting at about school age and progressing until you reach late adolescence. Others contend it is largely environmental, caused by too much "close work"—reading or other activities that force you to focus on nearby objects. The resting eye is focused on distant objects. In order to look at nearby objects, the lens of the eye must increase in thickness and decrease in radius of curvature. The eyes of myopic individuals are excessively long, so the image of an object forms in front of the retina rather than on it.

Some of the ophthalmologists who support the environmental hypothesis of myopia have tried to stabilize or slow down its progress by giving atropine eye drops to young children who show signs of becoming nearsighted. The atropine paralyzes the ciliary muscle, which controls the shape of the lens, and thus prevents the children from accommodating, or focusing on nearby objects. But the effects of this treatment are controversial.

Population studies seem to support, but not prove, the environmental hypothesis. A study at the beginning of the past century compared the eyesight of British guards to that of Oxford students and found a higher incidence of myopia among the students. A more recent study compared older and illiterate Eskimos to younger Eskimos who had learned to read and found that more of the younger Eskimos tended to be nearsighted.

More support for environmental causality came from experiments done in the 1960's by Francis Young at the Primate Research Center of Oregon State University. His experiments indicated that when monkeys' vision is restricted to a distance of 20 inches or less, they have a slight tendency to become myopic.

It is against this background that Wiesel and Raviola came upon their animal model of myopia. The work began 10 years ago, when Wiesel and his colleague David Hubel of Harvard Medical School were studying the effects of visual deprivation on the development of the visual system. In the course of their work, they would suture shut the eyes of young monkeys and then examine how the visual cortex developed. One day, says Raviola, Wiesel, who was then at Harvard, wandered into his office and remarked that the suturing experiments were producing a curious result. The closed eyes were nearsighted and grew much longer than normal, just like the eyes of most myopic people. He thought that the phenomenon could be clinically relevant, so he and Raviola, who is a retinal neurobiologist, decided to investigate the problem further.



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Monkey myopia

Diagram of a normal monkey eye superimposed on a nearsighted monkey eye. The nearsighted eye is longer.

"First, we wanted to rule out the possibility that the elongation of the eye was caused by a trivial effect of the closed lids," says Raviola. "Either the pressure exerted by the lids or a temperature increase in the orbit could interfere with postnatal eye development. If so, the phenomenon would have no meaningful relation to the human condition." The two investigators devised experiments to determine whether it was the effect of seeing distorted images through the sutured lids or local, physical effects of the suturing itself that was causing the myopia.

The closed monkey eyelids are very thin because the researchers remove much of the tissue underlying the skin of the lid when they do the suturing. For this reason, the visual experience of the monkeys is restricted to the perception of formless moving shadows when the animals are in the light. Wiesel and Raviola decided to suture shut the eyes of two groups of monkeys and rear one group in the light and the other group in darkness, where they would see nothing at all. The result was that the monkeys reared in light became nearsighted and the ones reared in darkness did not. They also took a group of young monkeys and made their corneas translucent by injecting small polystyrene beads into the corneal stroma. This technique also distorts what the monkeys see, without depriving them of light. Once again, the monkeys' eyes grew longer. "We concluded," says Raviola, "that the myopia was not caused by a local physical effect of lid closure, but was mediated by the nervous system."

Then Wiesel and Raviola looked back at the clinical literature to see whether visual distortion produces myopia in humans. They found that it does. "We found human conditions that resulted in myopia for which there was no previous explanation," says Raviola. For example, children with mild retrolental fibroplasia, a condition in which scar tissue forms over the retina, have distorted vision and are myopic. Children with corneal opacities tend to be myopic in the affected eye. More recently, it has been shown that children whose eyelids droop or who have hemangiomas of their eyelids develop myopia in the closed eye.

At that point, Wiesel and Raviola decided to analyze the mechanisms pro-

Slow Growth in Seabirds

Birds in the tropics that feed at great distances out to sea typically produce just one slowly growing chick per breeding season. By contrast, closely related species that feed nearshore usually rear broods of two or more rapidly growing chicks each season. The reason for the difference has long puzzled ecologists, although the most favored explanation has been that the single, slow-growing chick of pelagic birds is a reproductive adaptation to the more limited energy resources available in deep tropical waters as compared with nearshore. In a recent experiment on certain pelagic and nearshore bird species on the island of Midway, which is part of the Hawaiian group, Robert Ricklefs and R.E. Shea, of the University of Philadelphia, produced data that failed to support the energy limitation hypothesis (*1*). They suggest that, instead, the restrained reproductive strategy of pelagic birds is related to basic life-history characteristics that are rooted in rates of anatomical development. The ultimate question—why the difference?—therefore remains and is shifted to another arena.

The energy limitation hypopthesis has had many prominent proponents, including the late David Lack. It has had empirical support, too, in the form of twinning experiments, in which pelagic birds failed to raise two chicks when the brood had been artificially expanded. Ricklefs had earlier noted (*2*) that the growth period for pelagic sooty tern chicks is continuous and protracted, which is fueled by a steady energy requirement after an initial rise. By contrast, in the common tern, a nearshore feeder, the chick has a sharp peak in energy requirments midway through the growth period. One result is that the common tern fledges at 30 days, which is about half the time of the sooty tern.

These observations on energy requirements appear at first sight to support the energy limitation hypothesis until, that is, calculations are done on the energy budget effect of boosting the pelagic bird's growth rate. Ricklefs noted that a doubling of the growth rate of the sooty tern chick would increase its maximum energy requirement by only 20 percent. For the adult bird, the food-gathering burden would climb by only 5 percent, which seems inconsistent with the food limitation hypothesis.

Reasoning that doubling a pelagic bird's brood (as in the twinning experiments) was too severe a test, Ricklefs and his colleague decided to increase the feeding load of the pelagic gray-backed tern adult by replacing its chick with the larger chick of the sooty tern. Sooty tern chicks demand about 55 percent more food each day than their smaller counterparts, and finish up being 35 percent heavier. The question was, therefore, could the adult gray-backed terns meet these increased needs? Ricklefs and Shea substituted sooty tern eggs in ten gray-backed tern nests some 5 to 8 days prior to hatching and monitored the outcome.

Apart from three chicks that were lost within the first few days after hatching, the fostered sooty tern group survived and grew as well as a control sooty tern group: final body weights were not significantly different. The foster adults were apparently able to increase their foraging rate for their more active, faster growing chicks, and delivered 25 percent more meals than did a control group of gray-backed terns. From this, and some detailed statistical analysis of rate and bulk of meal delivery on specific days, Ricklefs and Shea were able to conclude that the energy limitation hypothesis fails to explain the reproductive differences between pelagic and nearshore species.

As a possible alternative source of explanation Ricklefs and Shea point to the significantly faster rate of maturation that is coupled with a lower growth rate of skeletal muscle in pelagic sooty terns as compared with nearshore common terns. The question of the single, slow-growing chick in pelagic birds might therefore turn on a need for precocial, rather than fast, growth: in other words, a question of life-history characteristics, not of simple energy budgets.—**ROGER LEWIN**

References

1. R. E. Shea and R. E. Ricklefs, *Am. Nat.* **126**, 116 (1985)
2. R. E. Ricklefs and S. C. White, *Auk* **98**, 361 (1981).

ducing myopia in the monkeys. The first question they asked was, Is it accommodation? They took young rhesus macaques and sutured shut one eye, leaving a tiny hole at the very periphery of the sutured lids so that the monkey could not see through the hole. They used the hole to introduce atropine ointment each day, thereby preventing accommodation. The treatment had no effect—the sutured eyes became nearsighted. Then they tried the same experiment with stump-tailed macaques. This time, the atropine prevented myopia from developing. It looked as though there might be more than one way to cause myopia, which may help explain why the use of atropine in children has had mixed results.

Raviola and Wiesel tried another type of experiment. They took a young rhesus monkey, sutured shut one eye, and cut its optic nerve, removing completely all visual imput from the retina to the brain. If myopia is a result of the eye's response to the distorted visual image received by the brain, this monkey should not develop myopia. But it did, indicating that the central nervous system is not involved. Then they repeated the same experiment with a stump-tailed monkey. The monkey developed almost no myopia.

"Why do these two closely related monkey species respond so differently?" asks Raviola. He and Wiesel postulate that the retina of the rhesus monkey may release a regulatory molecule that controls the growth of the eye. Perhaps when visual perception is distorted, this regulatory molecule could be released in abnormal amounts, thereby altering the growth of the eye. The myopia of the stump-tailed macaque, on the other hand, seems to result from the fact that its brain receives altered information and, in turn, causes excessive accommodation. Perhaps, the investigators speculate, both mechanisms are at work in humans, which could mean that the ophthalmologists who argue that close work causes myopia are correct. But genetic factors may also be important—for instance, some kind of wiring defect in the visual centers.

"What gives us satisfaction is that we are beginning to talk in terms of mechanisms, and we have shifted our attention from the growth of the eye to the nervous system. When we understand why myopia occurs, we might be able to think in terms of prevention," Raviola says.

—**GINA KOLATA**

Additional Reading

1. E. Raviola and T. N. Wiesel, *N. Eng. J. Med.* **312**, 1069 (1985).