bread. Bread and beans, in contrast, resulted in a slow rise in blood sugar more characteristic of beans than bread.

One immediate consequence of these results for diabetics is that the starch exchange lists of their diets, which are choices of equal carbohydrate portions of bread, rice, potatoes, or corn, are called into question. In addition, Olefsky points out, diabetics may want to know that some foods that they frequently avoid, such as ice cream, are fine as far as blood glucose is concerned. Olefsky remarks that he recently saw a new ice cream sweetened with sorbitol and labeled "not a low calorie food." The ice cream was aimed at diabetics. But regular ice cream gives a very flat glucose response. Marveling at the very existence of this dietetic dessert, Olefsky says, "Some major food company developed this product on the assumption that ice cream is bad for diabetics. Better they should go out and find a better potato."

Roth says it is his impression that the work of Crapo and Jenkins "is not widely known" and that "it is time for it to be considered" by diabetologists. Irving Spratt of the Spratt Diabetes Medical Clinic in San Bernadino, who is president of the American Diabetes Association, says the Diabetes Association is concerned about the possibility that the starch exchange lists may be misleading, that "we are considering changing the exchange lists and we will take appropriate action as all the evidence comes in." Crapo, he adds, is a member of the professional education committee of the American Diabetes Association. "We are in constant communication with Phyllis Crapo," Spratt says.

Studies of carbohydrates and their effects on blood glucose may help nutritionists understand public health issues as well as diabetes diets. Jenkins says he wonders whether the wholesale change in industrialized societies from foods like pasta, beans, and sweet potatoes to foods like bread, cereals, and white potatoes might be related to the prevalence of diabetes, heart disease, and some forms of cancer. He himself has begun eating pasta and beans since he discovered their effects on blood glucose. "It's a marvelous food anyway," he remarks.

Olefsky wonders whether there will be any large-scale health effects as food manufacturers switch from using sucrose as a sweetener to using corn syrup, which is less expensive. Corn syrup, which is mostly fructose, gives a very slow blood glucose response whereas sucrose gives a more rapid one.

The whole process of studying the blood glucose response of foods has been an eye-opener for nutritionists. They learned, says Crapo, that "What happens when we eat food is much more complex than anyone thought." Now that researchers are starting to look more carefully at their untested assumptions about food, Crapo predicts, "I think at last we will pull nutrition out of the dark ages."—**GINA KOLATA**

Additional Reading

1. D. J. A. Jenkins, R. H. Taylor, T. M. S. Wolever, "The diabetic diet, dietary carbohydrate and differences in digestibility," *Diabetologia* **23**, 477 (1982).

The Two Sides of the Brain

Behavioral asymmetries are linked to physical asymmetries in the brain; abnormal brain development may underlie learning disorders like dyslexia

At one time, cerebral dominance was thought to be a uniquely human trait. Only in humans, it was thought, is a particular activity or behavior such as speech under the primary control of one or the other of the brain hemispheres—a trait that is reflected by marked anatomical, chemical, and electrical asymmetries in the brain.

But now, as was repeatedly demonstrated at a recent conference in Boston on "The Biological Foundations of Cerebral Dominance," these brain asymmetries are being found in lower animals.* This gives researchers a way to study just what cerebral dominance means.

A major reason for the interest in these asymmetries is the association between childhood learning disorders and the development of anomalous dominance in the human brain. In most people, the left hemisphere has dominance over language abilities. But in a minority, the exact size of which is unknown, the right has gained at least partial dominance. These individuals are at higher risk of having language-related learning disorders, such as dyslexia, difficulty in learning to read.

More than a century has passed since certain behaviors were found to be more under the control of one brain hemisphere than the other. For example, in the early 1860's Pierre Paul Broca identified a region on the left side of the brain—Broca's area—that is important for speech control in most persons, especially right-handers. Left-handers are more likely to have some or all control of their language in the right hemisphere.

Until the late 1960's, the general consensus was that cerebral dominance existed independently of anatomical asymmetries in the brain. However, in 1968, Norman Geschwind and Walter Levitsky, who were then at Boston University School of Medicine, showed that easily observable differences, visible even to the naked eye, could be detected between structures in the left and right hemispheres.

Many asymmetries can be detected in the cortex, the outer layer of the brain and the site of such complex functions as language and control of voluntary actions. Geschwind and Levitsky found the planum temporale, a cortical area involved in speech, to be larger on the left hemisphere than on the right in about two-thirds of the brains examined. It was larger on the right in about 10 percent, and roughly the same size on both sides in the remaining brains.

More recently, Albert Galaburda and his colleagues at Harvard Medical School found additional speech areas to be larger in the left hemisphere of most brains than in the right. The language system as a whole may be asymmetric, he told the conference participants.

The asymmetries extend to the level of individual neurons, according to Arnold Scheibel of the University of California at Los Angeles. He described work from his laboratory that was undertaken to determine whether the dendritic structures of neurons from speech centers on the left side of the brain differed from those of corresponding neurons from the right hemisphere. The dendrites are neuronal projections that receive incoming

*The conference, which was held on 4 to 6 April, was sponsored by Harvard Medical School and the Institute for Child Development Research.

connections from other neurons. Greater dendritic length or complexity would imply more connections.

The UCLA workers obtained within 6 to 18 hours of autopsy the brains from eight male patients who had died of nonneurological causes. They compared individual neurons taken from Broca's area with neurons taken from a corresponding region of the right hemisphere and also compared neurons from the left and right precentral gyri. Whereas Broca's area may be considered strategic in that it is needed for the initiation and development of speech, the precentral gyri may be considered tactical because they control movements of the face and mouth.

The Scheibel group found that the total dendritic length of neurons from the strategic centers was greater than that of neurons from the tactical centers, a finding which may indicate that the strategic center neurons receive a greater neuronal input. Somewhat surprisingly, there was little difference in total dendritic length when neurons from either Broca's area or the left precentral gyrus were compared with corresponding neurons from the right hemisphere. There were indications of more complex branching patterns in the left-side neurons, however. "The total amounts of dendritic lengths were remarkably similar," Scheibel explains, "but there were more higher-order segments on the left than on the right." In brains from the two left-handers in the sample, the right-side neurons tended to have more higher-order branching.

Greater branching in neurons may be associated with greater complexity in information processing. Scheibel suggests that the dendritic patterns seen in these adult brains reflect differences in development in the two hemispheres during early life. But, he asks, "Does the dendritic ensemble grow after the dominance decision is made or is it the other way around?" He plans another study to characterize dendritic development during the first few years of life when language abilities are being acquired.

Asymmetries can be detected in the living human brain just as readily as in autopsy specimens, according to Marjorie LeMay of Harvard Medical School. For example, LeMay and her colleagues found the posterior end of the Sylvian fissure, which separates the frontal and temporal lobes of the brain, to be higher in the left hemispheres of most right-handed individuals, but higher in the right hemispheres of most left-handers. By examining computerized x-ray (CAT) scans, they also found that in most right-handers the frontal lobe of the right hemisphere is wider and extends farther forward than the left frontal lobe, whereas the left occipital lobe extends further to the rear. The two hemispheres of left-handers are often either more symmetrical than those of right-handers, or the asymmetries are reversed.

Moreover, LeMay and other investigators, including Ralph Holloway of Columbia University, have found similar asymmetries in the fossil skulls of early man and in the brains and skulls of the great apes and monkeys. "It seems pretty clear that the asymmetries have been developing over many millions of years," LeMay concludes.

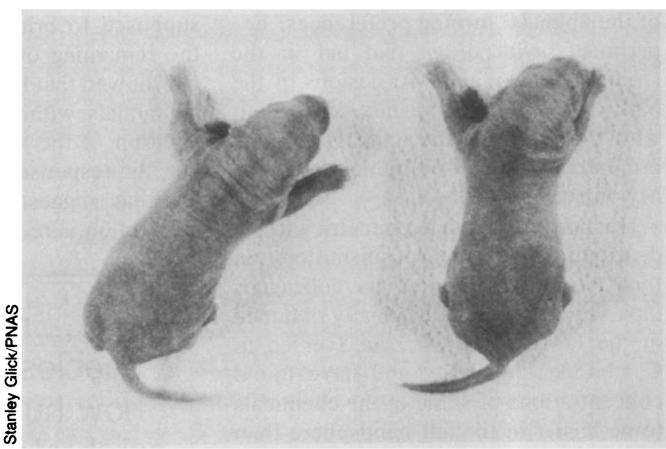
A long evolutionary history for brain asymmetry is supported by the finding of behavioral and anatomical asymmetries in the brains of animals, including birds and rats, that are lower on the evolutionary scale than nonhuman primates. Geschwind, who has been at Harvard Medical School since 1969, says, "It is now likely that no animal species, no matter how humble, lacks cerebral dominance."

Fernando Nottebohm of Rockefeller University has found that, in normal canaries, centers on the left side of the brain control the development of song (*Science*, 17 September 1982, p. 1125). However, contrary to the results with human and nonhuman primates and with rats, Nottebohm has detected no anatomical dissimilarities between the left and right song control centers that correlate with the functional asymmetry.

Anatomical asymmetries are present in the cortices of rat brains, according to Marian Diamond of the University of California at Berkeley. She has noted that in male rats the cortex is generally thicker on the right hemisphere than on the left, although the extent of the difference depends on the strain of the rat. In contrast, the left cortex of females tends to be somewhat thicker than the right, although the differences for the most part are not significant.

Patterns of asymmetry in human brains may also differ between the sexes. Males are more likely than females to have anomalous dominance for speech, to be left-handed, and to have speech-related learning disorders. Testosterone may be a factor in the development of brain asymmetries and anomalous dominance.

Sex hormones have been shown to affect the development of brain structures in animals. Nottebohm finds that female canaries can be induced to sing if their ovaries are removed and they are treated with testosterone, although they never sing as well as males. Testosterone causes a significant increase in the size of song control centers of the female birds when they are learning to sing.



Left- and right-tailed rat pups

The direction in which newborn rats turn their tails predicts their turning preferences later in life.

Stanley Glick/PNAS

The cortical asymmetries that were observed in rat brains by Diamond are also subject to hormonal influences. In experiments performed on Long-Evans rats, Diamond says, that "we are able to change the patterns in both males and females by removing the gonads at birth." As a result the male cortices became more like those of females and conversely.

Rats also display behavioral asymmetries. Normally active rats tend to run in circles. Stanley Glick and his colleagues at Mount Sinai School of Medicine in New York have found that individual animals have a preferential direction; some rats consistently prefer to turn right and others to turn left. The preference is established at a very early age. Some newborn rats consistently turn their tails to the left, whereas others turn their tails to the right. The tail positions assumed by the neonates predict the later turning preferences of the adult animals.

There is also a sex difference in this behavior. A population of female rats showed a statistically significant preference for turning to the right. Males showed no such marked preference, although there may have been a slight tendency to turn left.

The preferred direction of turn is related to a chemical imbalance in a region of the brain called the nigrostriatal pathway, which helps to regulate movements. "Each rat has a characteristic circling preference. There must be an endogenous substrate that mediates this asymmetrical behavior," Glick explains.

The neurons of the nigrostriatal pathway release the chemical transmitter dopamine. When the pathway is destroyed on one side of the brain, the animal turns in circles to the side of the lesion, that is, in the direction opposite to the intact dopamine-secreting side.

Glick and his colleagues have shown that in normal rats the dopamine concentrations are significantly higher in the side of the brain opposite to the direction of the animals' turning preferences. Experiments with drugs that act in the striatal pathway and with lesions of the pathway produced results consistent with the idea that the animals' turning preferences are caused by the dopamine asymmetry.

Humans also have asymmetries in the distributions of neurotransmitters in their brains. Glick and his colleagues have reanalyzed data originally obtained in the laboratory of Leslie Iversen at Cambridge University and have found concentrations of some of the chemicals to be higher in the left hemisphere than in corresponding regions in the right. The reverse was true for others. Particularly intriguing was the observation that dopamine concentrations were higher in the human nigrostriatal pathway on the side contralateral to that of the individuals' hand preferences. This result is consistent with the rat data.

Victor Denenberg described experiments performed in his laboratory on the effects of environmental simulation during early life on behavioral and brain asymmetries in rats. The experiments were aimed at testing the hypothesis that early experiences are stored in the right hemisphere.

The Denenberg group compared the performances of adult rats that were not handled during the first 21 days after birth with animals that were. Early handling altered the behavior of the animals in a number of tests. For example, control males did not show an overall preference for turning one way or the other, but handled males had a marked preference for turning left. Handling also reduced the tendency of male rats to kill mice. Experiments in which either hemisphere was destroyed before testing the animals led to the conclusion that the brain changes that produced the altered behaviors in handled rats occurred in the right hemisphere, as predicted.

Ida Gerendai of Semmelweis University Medical School in Budapest, Hungary, has been exploring interactions between the brain and a number of endocrine glands. Her results suggest that the brain, in addition to regulating endocrine function with neurohormones that are released by the hypothalamus, can do so by direct neural connections to glands, including the thyroid and the ovary.

When one ovary is removed, the normal response is for the other to grow larger. This was thought to be caused by the increased release of hypothalamic neurohormones that is evoked by the reduction in ovarian hormones. The neurohormones in turn stimulate release of pituitary hormones, which were then supposed to bring about the growth of the remaining ovary. However, Gerendai showed that the increase occurs even in animals without pituitary glands. In addition, if the nerves to the ovary are cut, the response does not occur, a finding that suggests that a direct neural connection is required.

> "... no animal species, no matter how humble, lacks cerebral dominance."

The neural control may be asymmetric. Gerendai finds the concentration of luteinizing hormone releasing hormone, one of the hypothalamic neurohormones, to be higher in the right side of the hypothalamus in intact rats. When she removes one ovary and also destroys the right locus coeruleus, a brain region involved in regulating the ovary, the usual size increase does not occur in the remaining ovary. Destroying the left locus coeruleus does not prevent the response.

Neuroscientists are clearly finding a wide range of behavioral, chemical, and anatomical asymmetries of the brain. The next question is whether alterations in the development of these asymmetries can lead to anomalous dominance and learning disorders.

For many years there were thought to be no anatomical abnormalities in the brains of individuals who have learning disorders such as dyslexia. But, within the past few years, Galaburda and Thomas Kemper of Boston University School of Medicine identified changes in the cellular architecture of the brains of dyslexic patients, which may be the result of slowed development of the left hemisphere of these individuals. In addition, Frank Duffy of Harvard Medical School has shown that electrical responses to certain stimuli are different in the brains of dyslexic patients than in normal controls.

At the Boston meeting, Patricia Goldman-Rakic of Yale University School of Medicine described an experimental approach for investigating brain development that may shed some light on the situation. The approach, which was developed in collaboration with Pasko Rakic, who is also at Yale, is to alter normal brain development by performing surgery on the brains of nonhuman primate fetuses. According to Goldman-Rakic, altering one region of the developing brain can have profound effects in others. Neurons may grow to an abnormal part of the brain if their normal target is removed. Or the neurons of one pathway may form more connections with a particular target if another incoming pathway is disrupted. In addition, removing one portion of the developing brain allows another to grow much larger than normal.

As already mentioned, testosterone is one of the factors that affects the development of brain asymmetries. Testosterone action may also help to explain a surprising observation made last year by Geschwind and Peter Behan of the University of Glasgow. They found that left-handedness is not only linked to an increased incidence of language disorders, which was already known, but also to an increased incidence of autoimmune disease and migraine headaches (*Science*, 9 July 1982, p. 141).

In autoimmunity, the body's immune system inappropriately attacks its own tissues. A link between an immune defect and neurological dysfunction was unexpected to say the least. But as Behan and Geschwind reported in Boston, further investigation continues to confirm the linkage. Behan and Geschwind postulate that, in addition to affecting brain development, excess testosterone production in some fetuses acts to suppress development of the thymus gland, which is needed for normal immunity. As a result, autoimmunity eventually develops.

Whether or not this proves out in the long run, neuroscientists have come a long way in their analysis of brain asymmetries and now at least have the tools for studying the learning disorders.

—JEAN L. MARX