Is it your brain that makes you male or female?

● No one would dispute that most little girls play with dolls and that most boys fight. But *why* do the sexes behave differently? Some scientists—and most feminists—would answer that boys are conditioned to be tough and competitive, girls to be soft and "feminine." Evidence is accumulating, however, that there are also inborn differences between the brains of males and females. In computer terms, they may be wired up differently by nature as well as being programmed differently by society. BRYAN SILCOCK reports

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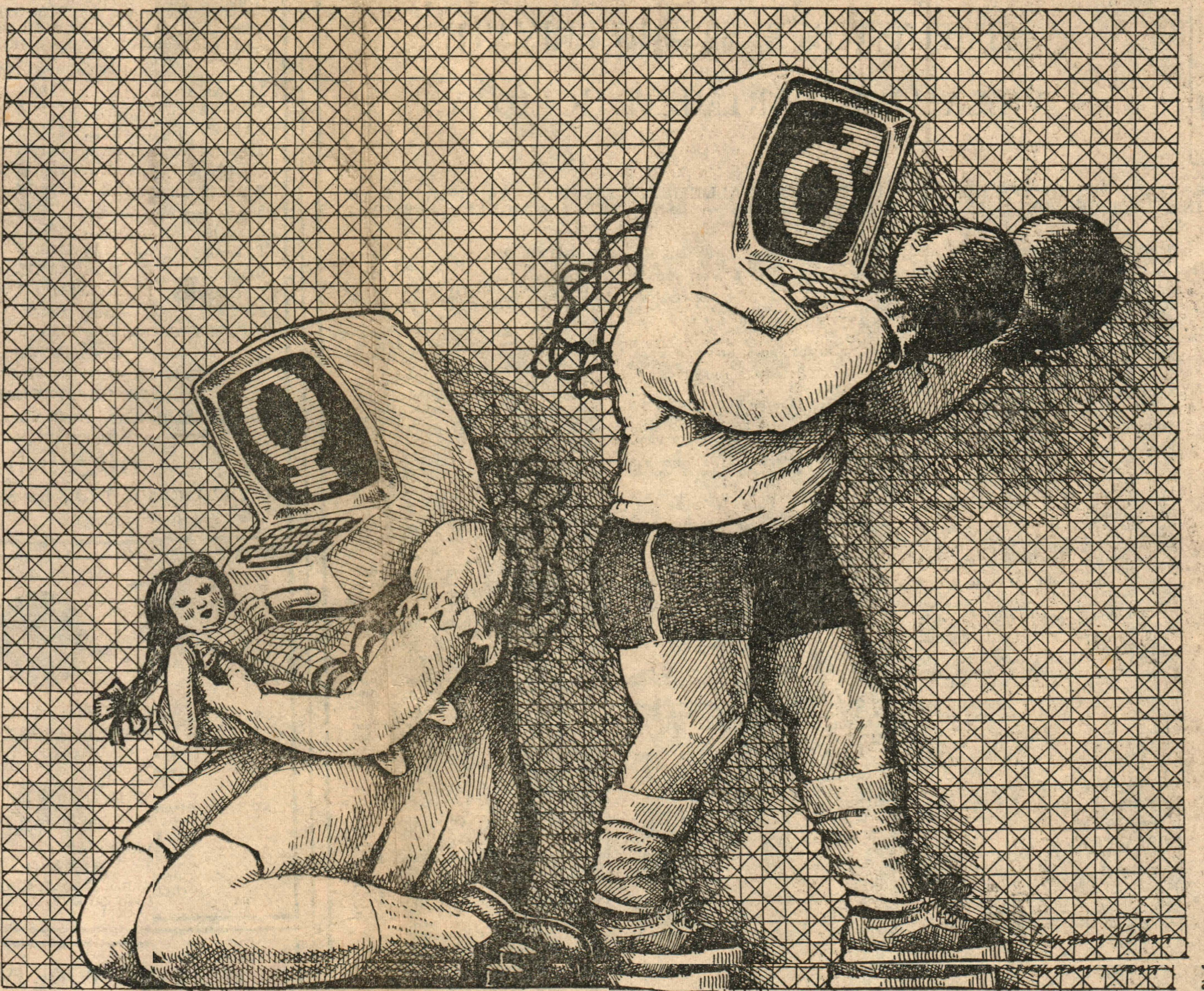

IN A REMOTE corner of the Dominican Republic, genetic bad luck and inbreeding have combined to make a rare form of ambiguous sex relatively common. Those who suffer from it are usually taken at birth to be girls and are reared as such. But, as puberty approaches, odd things start to happen. Their voices deepen, they develop male genitals and musculature. They take an interest in girls and they gradually slip into male roles. Many eventually marry. Some become fathers.

After this condition had been identified a few years ago, isolated cases soon began to be recognised outside the Dominician Republic—in fact, all over the world. And another curious aspect emerged. As Professor Michael Besser of St Bartholomew's Hospital in London explains: "They often begin to *think* of themselves as boys at the age of five or six, long before any physical changes occur."

This challenges the hitherto generally accepted view that gender identity—the basic "I am male" or "I am female" assumption everyone makes about themselves—is fixed early in life by sex of upbringing, that is, by the way we are reared. Could it be that, despite their apparently female bodies, these Dominicans' brains are male from birth?

Most experts in the field would now agree that a very strong argument can be made for this view. The direct evidence is patchy, as it nearly all comes from rare cases of ambivalent sex like those in the Dominican Republic. These "natural experiments" are the only way of disentangling the effects of nature and nurture in humans. But they are underpinned by an impressive body of evidence from animal experiments.

And, if the animal analogy is valid, this is what happens: just before or just after birth, sex hormones circulating in the blood of boys affect the brain, producing anatomical differences from the female brain in the form of a different pattern of connections between nerve cells.

The sex hormones have this effect only during this brief, critical period, and the pattern, once established, cannot be changed. (In this respect the brain differences are unlike some physical differences between males and females which can be modified in later life, by hormone treatment, for instance).

Differences in the "wiring" of the male and female brain would be expected to express themselves in different ways. As well as helping to account for such behavioural differences as those illustrated, the different wiring could also explain different mental aptitudes—why, for example, men tend to be better than women at mathematics and women tend to do better in tests of verbal skill.

So what is the evidence for the "wiring" theory?

THE PROCESS of sexual differentiation begins as early as the moment of conception — although to start with the male and female foetuses are remarkably alike.

In mammals the sex of the offspring is determined by the father. Each sperm carries, as part of its package of hereditary material, either an **X** or a **Y** chromosome. When a sperm fertilises an egg the result will be genetically male if the former carries a **Y** chromosome, female if it carries an **X**.

The basic sex is female

But, for the first month of pregnancy, male and female embryos are virtually identical. Even during the second month differences are confined to small changes in the bunch of cells that will eventually become gonads—the ovaries in females, the testes in males.

It is only around the beginning of the third month, when the embryonic testes start to produce androgens—male sex hormones of which testosterone is the most important—that differences in the other reproductive organs begin to appear. Without androgens, development of the foetus is along female lines. So it can be said that the basic sex of mammals is female, and the male is a variation from the norm. (In birds it is the other way round.)

The vital role that hormones play in sexual differentiation has been recognised for a long time. It began to be elucidated about 30 years ago when scientists started to manipulate the early hormonal environment of experimental animals. Working mainly with rats, rabbits, and guinea pigs, they castrated males before, or immediately after, birth (thus stopping their supply of androgens); and they exposed young females still in the womb to androgens.

The scientists found that they could thus produce, almost at will, various odd physical combinations: genetic females with ovaries and male genitals, genetic males with testes and female genitals, and all sorts of intermediate stages.

But it soon became clear that sometimes it was not only the animals' reproductive organs that were being changed by sex hormones. Their behaviour patterns in later life showed that their brains could be affected too.

In such cases, it emerged, the *timing* of the hormone experiment was absolutely crucial. Physically normal female rats exposed to androgens immediately after birth would behave like males as they matured, fighting for dominance and trying to mount females. Similarly, males castrated at birth would later show female patterns of sexual behaviour. But the same hormone treatment given earlier or later would not produce these behavioural effects.

The evidence of brain differences between the sexes is not confined to behaviour patterns. In some animals it is possible to see anatomical differences in the male and female brains. In rats, for instance, an experienced observer can tell the sex from the size of various cell clusters in a part of the brain called the hypothalamus. And with an electron microscope, the pattern of connections between the nerve cells in these clusters can be seen to be different in males and females. Experiments have shown that the pattern depends on the hormones the new-born animal was exposed to.

In canaries similar cell clusters can even be associated with a particular function—the ability to sing. In males, which sing, they are large; in females, which do not sing, they are small. But, if female canaries are given masculinising hormones after hatching, the clusters enlarge, and the birds start to sing like males.

RODENTS and canaries are a long way from humans, of course. What about larger mammals?

Some of the most impressive research here has been provided by Professor Roger Short, who directs the Medical Research Council's Reproductive Biology Unit in Edinburgh, and has worked with sheep, and wild red deer on the island of Rhum.

In one experiment with deer he found that a male castrated at birth never left its mother. It was accepted as female by stags in the rutting season and not chased away as a young male would be. But surprisingly, this castrated male still tried to mount its mother. The normal trigger for male sexual behaviour is the production of testosterone, but this animal produced none. The best explanation for its mounting attempts seems to be that its brain had been imprinted before birth with a specifically male pattern of response to a female in season.

Short's experiments with sheep are equally intriguing. He treated ewes at various stages of pregnancy with testosterone and then reared the lambs. One effect he discovered was that when female lambs produced in this way grew up, they could be made fiercely aggressive, capable of chasing off a good-sized dog, by a dose of steroid sex hormones whose effect on a normal female would be merely to produce ovulation. In these cases the hormones were working on masculinised brains.

The mammal experiments that shed most light on man are, however, those involving monkeys. And here it emerges that the processes are more complicated. Patterns of sexual behaviour can still be switched by carefully timed exposure to hormones around the time of birth, but there is an important distinction from the lower animals. If you dose female rats and sheep with androgens you can not only make them behave like males; they can also lose a crucial female attribute—the ability to produce the hormonal response that leads to ovulation.

Similar treatment of monkeys, however, will have the first effect but not the second. The implication of this is that, as we move closer to man up the evolutionary tree, the effects of sex hormones on the brain become less far-reaching.

Nevertheless, there is no doubt that there are some effects on the monkey brain. Does this hold true for humans?

THE PRACTICAL difficulty in trying to answer this question is obvious: scientists cannot carry out deliberate, controlled experiments on humans. So the information can come only from freakish "natural experiments" like the Dominican Republic cases, and from the unintended side-effects that sometimes occur when hormones are used in medicine.

What usually happens in the "natural experiments" is that genetic defects lead either to abnormal hormone production, or to an abnormal response to them by the body. In the Dominican condition, for instance, there is an inborn inability to convert testosterone to a more potent form called dihydroxy testosterone (DHT).

Lack of male development

And without DHT, normal masculinisation does not occur in the foetus. But a crucial part of the brain appears to be sensitive to testosterone and becomes male. However the lack of male development is corrected at puberty, when there is so much testosterone around that masculinisation occurs without conversion to the more potent DHT. So the body is brought into line with the presumed masculine brain.

There is a feminine analogy to this, provided by another human genetic defect which mimics the animal experiments in which females are exposed to testosterone around the time of birth. In these cases there is a missing link in one of the chemical production lines in the adrenal glands. As a result the chemical products that precede the missing link pile up, and to get rid of them, the body converts them to androgens. With a male baby this produces changes of puberty in infancy — so-called infant Hercules. With a female baby it can cause masculinisation of the genitals. Sometimes it proceeds so far that the babies have penises and are brought up as boys.

If this genetic defect is recognised at birth, its outward masculinising effects can be corrected by surgery and hormone treatment and the children brought up as girls. If such "corrected" females show a tendency towards male behaviour, it is unlikely to be the result of social conditioning. The most likely explanation would be that the brain received some form of male imprint before birth.

Similar individuals have also been produced by medical accidents. Hormones are sometimes used when a woman is threatened with a miscarriage. When this kind of treatment was first introduced synthetic hormones with unexpected masculinising effects were occasionally employed. As a result, partly masculinised female bodies were produced.

BUT HOW is a masculinised or feminised human brain in a body of the opposite sex to be recognised? You can hardly measure the number of mounting attempts in humans. Scientists are, therefore, forced back on much vaguer kinds of evidence.

They have identified three aspects of human sex-related behaviour that seem relevant. First, gender identity—the sex an individual thinks he or she is. Second, gender role, as expressed by such things as rough and tumble play or an interest in dolls. This is not the same as gender identity. For instance, a tomboy has no doubts that she is a girl but she still acts boyishly. Finally there is sexual preference—an individual's preference for heterosexual or homosexual relationships —or for both.

Studies of gender identity have not shed much light on the question but studies of gender role do provide very positive evidence that there are sex differences in the human brain. Several American studies have shown that when girls who were exposed to prenatal androgens are compared with carefully matched normal girls the former are consistently more male in their behaviour. They go in for more rough and tumble play, associate more with boys, think of themselves as tomboys, are less interested in dolls and more interested in careers. There are even indications that they are more aggressive.

As for sexual preference, a few scientists have speculated that homosexuality might be a product of early hormonal influences on the brain. An eminent East German doctor, Gunter Dörner, is convinced that low levels of male sex hormones during pregnancy contribute to male homosexuality. He has even persuaded his country's medical authorities that hormone levels in pregnancy should be monitored and artificially raised if low as a measure to reduce the incidence of male homosexuality.

But most Western experts are deeply sceptical of Dörner's theories, and of the experimental results on which they are based. They are horrified by the idea of basing any kind of therapy on them.

Apart from Dörner's results, the only evidence for any effect of prenatal hormones on human sexual preferences is a slightly above average incidence of bisexuality among women who were exposed to androgens before birth. No one has been able to establish any connection with transsexualism.

Nevertheless, the most reasonable interpretation of the animal and human studies is that nature—the "wirer" of the brain—has a significant role alongside nurture — the "programmer"—in deciding how the two sexes behave.

It is a fascinating finding and one that feminists may find provocative. For one of the practical conclusions that can be drawn from it is that it may be more difficult to change those sexual stereotypes than some people like to imagine.