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Figs, Steroids, and Feedback Loops

A revised theory of inheritance explains many human mysteries: why are we so different from our closest animal relatives, how our brains became so large but then started to shrink, and why the two sides of our brains apparently have different functions. We find that far from a continued advance, the human system has suffered a stall in its development, and this has affected our health, how we feel, and even how we behave. Identifying this problem is the first stage of finding a solution.

THE CORE HYPOTHESIS

There is no satisfactory explanation for why humans are physically, mentally, and culturally so very different from bonobos, chimpanzees, and gorillas when as far as our genetic blueprint is concerned we are all nearly identical. Chimpanzees are genetically closer to us than they are even to gorillas, despite their closer physical resemblance. The uniqueness of humans, therefore, requires a serious explanation that does not strain our credulity by invoking "outerworld" concepts that can never be proved or tested. We suggest that the unique features of human

evolution and our expanded consciousness can be best explained by a mechanism that acted slowly over the millions of years of primate evolution but, somewhere down the ape and hominid lineage, started to skyrocket. This mechanism was driven by the biochemistry of a predominantly plant-based diet that acted on the steroid hormone environment of the animal in a way that altered steroid activity.

So what are steroids, and why are they so important? Steroids are fat-soluble organic compounds that occur naturally throughout the plant and animal kingdoms. They include molecules like cholesterol, which in animals are transformed by a series of biochemical steps into specific hormones. For example, enzymes in the male and female reproductive organs change cholesterol into the familiar sex hormones—testosterone, progesterone, and the estrogens. Other enzymes convert cholesterol into other kinds of steroid hormones, such as cortisol, which is secreted by the outer layer of the adrenal glands in response to stress. These steroid hormones pass through cell walls and act deep within the cells, in the nucleus, where they regulate the transcription (the reading) of various genes. Transcription followed by the translation process (the "writing" of that gene) results in the construction of proteins, and these are the building blocks of our cells (structural proteins) and the chemicals that run them (enzymes) (see figure 3.1).

Hormones alter cellular operations by changing the types, activities, or quantities of important enzymes and structural proteins. They can stimulate the synthesis of proteins and enzymes, they can affect the activity of enzymes by turning them on or off, and they can increase the rate at which the various proteins and enzymes are made. By these mechanisms, hormones can modify the physical structure and biochemical properties of the cellular system. Hormones are a fundamental part of our functioning; our very structure depends on them.

Steroid hormones in particular are an integral part of the mechanism that reads the DNA, the blueprint that ultimately dictates the structure and chemistry of what is built in the body and ultimately how it works. To make this clear we can consider the different developmental pathways that lead to a person being male or female.

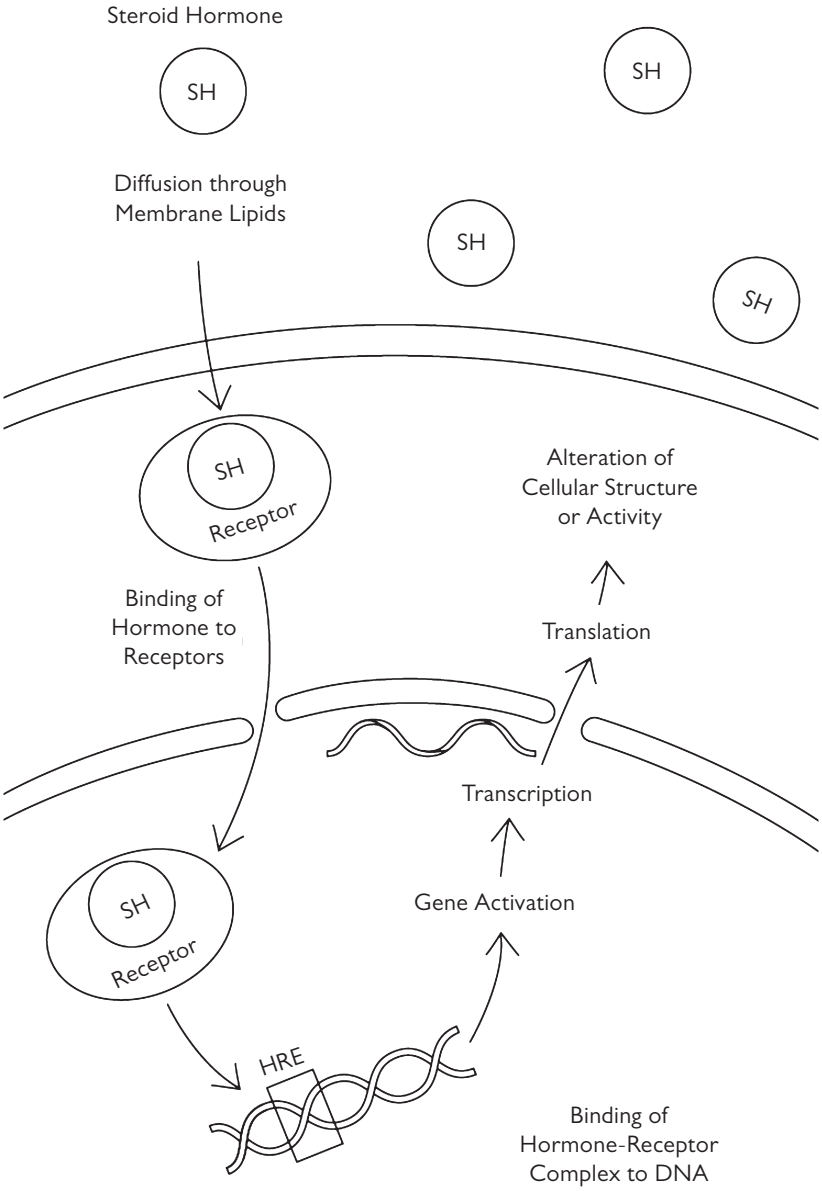

Figure 3.1. This diagram illustrates the basic transcription process and highlights the role that steroids play.

If a developing fetus has a Y chromosome, it will become a male; otherwise it defaults to the female developmental pathway. The Y chromosome's primary purpose is to initiate the production of a protein called testes-determining factor, which induces undifferentiated fetal gonadal cells to develop into testes. Once this occurs sexual dimorphism is not driven by the presence or absence of the Y chromosome but by the chemicals secreted by the testes. These include a peptide hormone, which inhibits the development of a female reproductive tract, and the steroid hormone testosterone (together with the closely related estradiol), which effects changes in the neural structure of the fetus and directs the masculinization of the entire body.

Once the DNA has set the developmental pathway in motion, the Y chromosome no longer has a significant role. It is the hormones that actually effect the changes. Their importance cannot be over emphasized.

In transcription the key players are the code (DNA), the reading equipment (ribosomes), and the steroid hormones, which, in simple language, tell the ribosomes what to read. At puberty the steroid hormones tell the ribosomes to read the code differently from before, and what results (in males) is a new structure with a bigger chest and more body hair. It's the amount or activity of the steroid hormones that dictates what happens. Steroids are extremely powerful chemicals. Minute changes in the levels of steroids in the body can have a big effect. Any external or internal factor that changes the balance of these chemicals can have major consequences. We can see from individuals wishing to change sex that even after the body is built and mature, taking more or less of a particular hormone can result in structural changes. Establishing a different hormonal regime can, for example, result in men growing breasts. The DNA code has remained the same, but the structure of the body has changed.

There is a major degree of plasticity within this building mechanism, and this is at its greatest in the earliest stages of human growth and development. The effects of an abnormal hormonal environment during pregnancy have been well documented. For example, in cases in which the fetus is female and the mother, for whatever reason, has

expressed abnormally high male hormone levels, fetuses have been known to develop pseudomale genitalia. These aberrations can be treated by surgery and hormone therapy after birth, but such androgenized girls also display a whole host of masculine behaviors as they are growing up. They have been found to expend significantly more energy during play than other girls, prefer boys as playmates, engage in more fighting, and have much less interest in dolls, playing motherhood, makeup, and clothes. This plainly demonstrates not only how structure can be altered by a change in the balance of an individual's steroid hormones, but also how an altered balance of a mother's hormones can affect her baby permanently.

Since the elucidation of the DNA molecule, a great deal of attention has been focused on its central role as a blueprint for growth, development, and functioning, as well as the evolution of higher organisms. But on its own, DNA is of no more use than is the hard disc of a computer. If anything, it is the equipment that reads the disc that is more complex and central to the end result. We need to remind ourselves that in considering the evolution of the biological system, the interaction between DNA and the transcription system is a more useful framework than just DNA on its own. Once such a framework is established as possible, a significant variation on the standard model becomes evident.

DNA is usually thought to be the only conveyance for the passage of information to the next generation and hence to variation, adaptation, and evolution. The mechanism that reads the DNA is assumed to be stable. This is not usually included in the picture as far as inherited change and variation are concerned. The standard evolutionary model is based on the changes that come from glitches in the DNA code. These changes are taken to be accidental (e.g., mutation) and usually deleterious, but when they are of benefit, the benefits incurred will create a fitter animal with enhanced survivability (e.g., selection). However, there could be, theoretically at least, a secondary mechanism for inheritance. If variations in "what is built" within an animal's lifetime somehow affect how the DNA is read, then these slight differences may be built into the structure of an offspring in the next generation.

We propose that something acting on the functioning of this mechanism gave rise to the unique features of primate evolution, eventually reaching its maximum expression in humans. Without contradicting accepted biology, a case is presented for externally driven steroid and monoamine oxidase (MAO) inhibition as the significant missing piece of a puzzling jigsaw. (MAO is a key enzyme that regulates neurotransmitter activity by breaking down key neurotransmitters.) The importance of this has not been fully explored before because of the continued emphasis on DNA as the only variable part of the evolutionary inheritance mechanism.

Loops within Loops

A fundamental property of our, and all animals', biochemical systems is their extreme delicacy; only a very small amount of chemical change can have a profound affect on function (as we can see from the contraceptive pill). If the diet of our primate ancestors in the tropical forests was full of biochemically active material, some effect was inevitable. As many of the chemicals in fruit are known to modify steroid activity, it is very reasonable to suppose that over millions of years, they were responsible, or at least partially responsible, for many changes to functions, like the timing of sexual maturation.

The way hormones, steroids, and the DNA reading mechanism function are complex, for they interact within a web of interdependent loops. The neural network and ultimately the brain are significantly involved as well. The glands, which produce the hormones, were once thought to run independently, with the levels of production self-regulating, that is, the hormones themselves regulating hormone levels, but now specific neural pathways have been found to end in the glands. These are believed to directly stimulate the production of hormones; the glands are thus not autonomous. The neural system runs or at least modulates the hormone system. There is a tendency within orthodox science to the belief that discrete systems work in isolation. This is due in part to the way subjects are studied in isolation. (The study of the ductless glands and their secretions is termed endocrinology.) But now there is an absolute acceptance

of the link between the neural and endocrine systems, so much so that this branch of investigation is now labeled neuroendocrinology. We now know that the brain affects the hormone system, which in turn regulates the DNA reading, which in turn influences the animals' structure and the mechanism of construction.

This is important, for slight changes in the construction of the brain could affect the modulation of the hormone system. An altered brain, for example, could result in an increase or decrease in the quantity of hormones, like melatonin, that the pineal gland produces.

A Progressive Hormonal Effect

Though these interconnecting factors are far from simple, so far we have shown the importance of steroids as regulators of DNA transcription and how the levels of steroid sex hormones can affect major changes in the body. We have noted the sensitivity of the body's systems to these powerful chemicals and pointed out that the brain is connected to the hormone-producing mechanism. We have also considered how an external factor, such as diet, can affect the levels, or at least the activity, of these substances in the body. We will now show how these factors could have played a part in the evolution of our big brains via a hormonal effect initiated in one generation creating more of the same effect in the next.

In the uterus the hormonal environment provided by the mother affects how the fetus is built by acting on its DNA-reading mechanism. The neural and endocrine systems of the fetus will be changed by this mechanism. Furthermore, a variation in the building program will not only affect the function of these systems in that individual's lifetime, but could also affect the next generation as well, because if the offspring is a girl, it could alter her own future uterine environment.

The changes brought about by an altered hormonal environment in the uterus will be concrete and structural. What is constructed in the baby in, say, Weeks 3, 7, and 9 of pregnancy will be lasting. This offspring will have a different structure and function from its parents due to the different hormonal-chemical balance it was exposed to during

gestation. The big variable here is the reading mechanism, not the DNA code. We have seen in examples, such as the physical changes that occur at puberty, how central the reading mechanism is to structure. It is not the code that is changing at these times, it is how the DNA code is read, and this is chemically influenced. The way steroids act is the variable link in this mechanism. This is a crucial piece of our hypothesis, so in the interests of clarity, we will run through this once more in a slightly different way.

If, for example, a pregnant woman has a slightly abnormal hormone regime, it would be this regime that courses through the body of her fetus. The growth and development of the fetus would be slightly changed in response to this altered regime. Even though its DNA code is unique, the growing child is not an autonomous unit growing in isolation. In the uterus she (and it is the female line that is significant) is being flooded with her mother's hormones, and this will have some effect on aspects of how she is built.

There could be a number of slight changes brought about by this hormonal effect, but for our theory we need to focus on the possibility that it is the fetus's neuroendocrine system and hence its DNA-reading mechanism that is modified. These structural modifications would then be with that individual for its entire lifetime. This is of particular importance, for the neuroendocrine system would affect the growth and development of the child, including potentially the length of the juvenile period, the timing of puberty, and how her brain functions. It would also affect the hormonal environment in her uterus when she conceives. The hormonal regime that floods her uterus would be different from that of her mother because she would have a neuroendocrine system that is structurally different. She would pass her normal, unchanged (by this mechanism) DNA to her offspring, but, from Day 1 in the uterus, the new fetus would develop in a slightly more altered hormone environment, which would again affect how its neuroendocrine system and DNA-reading mechanisms are built.

The DNA would not be altered by this mechanism, but there would be an effective DNA change because what is built is dependent

on how the DNA is interpreted. If these changes were all generally flowing in the same direction, what would be built could change progressively over the generations.

There could have been thousands of different variations within this overall framework that went nowhere, but if in one lineage there was an inhibition of steroid activity that in turn led to more steroid inhibition through subsequent generations, this one variation could have led to lasting change. If such structural changes resulted in the production of, for example, more melatonin and a modified steroid environment, the loop could start running faster. More melatonin and less steroid activity boosts this process because melatonin suppresses steroid activity and reduced steroid activity takes the brakes off melatonin production.

Such changes could lengthen the juvenile period. And because neural development, in effect, stops at puberty, a longer juvenile period allows more time for the development of the brain and, indeed, the neuroendocrine system. It is theoretically possible then that this longer window of development boosted pineal activity and hence melatonin production, affected the neuroendocrine system, and had an enhancing effect on the uterine environment eventually provided for that person's developing child.

These are key factors. The mechanism will only work if these related factors flow in the same direction—in the direction of suppression of steroid activity. It is also necessary for there to be an incremental increase with every generation. This may perhaps seem unlikely, but we are trying to explain an unlikely developmental event—the production of a uniquely big-brained primate. All we need for a fast-track mechanism to get up and running is the DNA-reading system to change in a way that produces ever less steroid activity.

A NEW THEORY OF INHERITANCE

What we are proposing here is nothing less than a new theory of inherited and evolutionary traits. The standard model is totally DNA based—inherited traits are passed on via DNA codes—but if a different

reading system can be inherited and passed on, there is, in effect, a transmission of a different DNA expression. The DNA and the reading system do not work in isolation. They go together. The reading system is built in the uterus. A change in this reading system will result in different structures, including the structures that read the DNA. If these are stable, the way the DNA is read will be changed permanently. This is a new and radical theory that has huge implications. It is a mechanism for inheritance that does not depend on changes in the DNA. It is an inherited reading change.

This theory is not incompatible with the standard DNA model for inheritance. It is merely a variation that, we propose, had a marked effect on the evolution of the ape and hominid lineage. The key point is that the variation is coming from the neuroendocrine system, and it is this variation that is inherited. However, this does not preclude DNA variation working with, alongside, in response to, or independent of this mechanism.

This mechanism is really very straightforward, and it is surprising it hasn't been identified before. At its simplest, we can see that as we grow, our DNA transcription system builds the brain. The brain regulates the hormone system, and the hormone system, particularly the steroid hormone system, is part of the mechanism for DNA transcription. This forms a circular loop. Anything entering this loop, for instance a biochemical influence from a fruit diet, could affect all parts of it in the following ways:

A. Steroid inhibition directly affects transcription. An individual growing and developing in an altered-transcription environment would be built slightly differently. This difference would include an altered brain. As we have seen, the brain modulates the hormone system. If the altered brain affected this modulation in a way that suppressed steroid activity, a loop of progressive effects could be established.
B. The individual's juvenile period would be extended due to the direct effects of the sustained steroid-suppressing chemicals. An

extended juvenile period would allow for a longer period of brain growth, as steroid hormone activity at puberty brings to an end the neural development. This could again lead to a slightly different brain structure and function.

C. The direct effects of a fruit diet, rich in MAO inhibitors, are likely to stimulate greater pineal activity. The pineal would produce more melatonin and beta-carbolines. These chemicals have a similar effect to the chemicals found in fruit. They suppress steroid activity.

Any neural changes created by this mechanism would initially have been very slight, indeed minuscule, in any one generation. If, however, a buildup of changes caused the pineal to produce more chemicals that reinforced the external chemical effect, then the rate of change could increase. We propose that this loop of changes built to a point in which the pineal had the dominant effect. So, while this process would still have been underpinned by a fruit diet that provided continuing supplies of steroid-suppressing chemicals, the predominant effect became increased pineal activity. This significant biochemical change could have created an internal environment that, via the stages we have elucidated, produced an even larger brain with enhanced functions as well as the potential for a slightly bigger brain with each successive generation (see figure 3.2).

Over the last few million years, there was a slow increase in neural capacity in primates, largely we believe as a result of increasing pineal activity initiated by a diet rich in fruit. In the human line the pace of expansion quickened. There was a doubling of brain size in a very short time. The biochemistry of plants has a lot to answer for.

CHEMICALS IN PLANTS

Plants in general, and their fruits in particular, contain a very large number of chemicals. They could with great justification be called biochemical factories. Many of these chemicals are similar to ones within the human body and can affect how our internal biochemistry works.

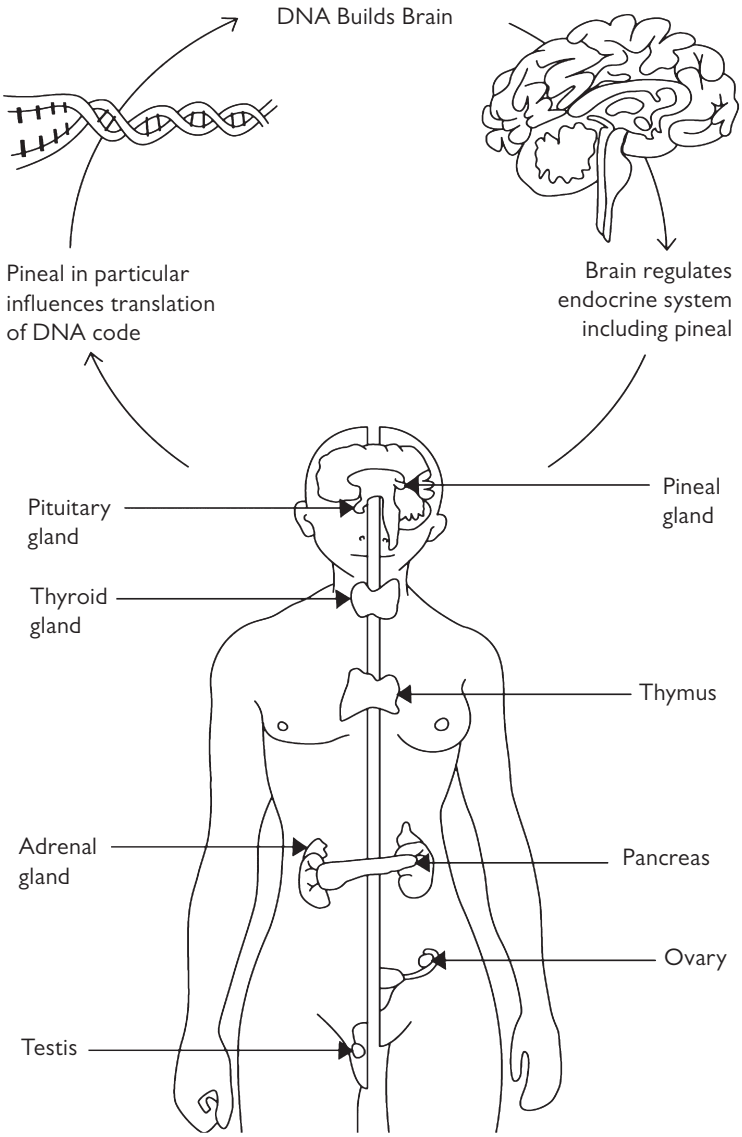

Figure 3.2. This diagram shows the major players in the transcription mechanism. The DNA code builds the brain, the brain regulates the hormone (endocrine) system, and the endocrine system regulates steroid activity. In most higher organisms the neuroendocrine system is a fairly stable part of the mechanism; changes that occur originate in the DNA code.

There is a close correspondence between plant and animal biochemistry, which is why we use plants for healing and as the basis for many pharmaceutical medicines.

Two new breast cancer drugs, tamoxifen and exemestane, are close to being synthetic equivalents of plant chemicals called flavonoids. Exemestane works by blocking the action of the enzyme aromatase, which converts androgens into estrogens. Tamoxifen directly inhibits the activity of estrogen. As most breast cancer cells need estrogens to divide and grow, these actions can stop cancer growth and even cause tumors to shrink. In the development of the drugs it was found that some naturally occurring flavonoids could also powerfully inhibit the action of aromatase.

Another study further emphasizes the power of flavonoids. Professor Richard Sharpe, senior scientist at the Medical Research Council's Human Reproductive Sciences Unit in Edinburgh, was concerned about the potential effects on babies of endocrine-disrupting flavonoids in soy milk formula. Marmosets were used in the trials as they have a similar endocrine system to humans. The study showed that simply feeding them a flavonoid-rich diet postnatally was enough to severely inhibit the neonatal testosterone surge. (In humans this surge has been linked to neural development and synaptic pruning.) Though this study is ongoing, initial findings suggest that the marmosets are not adversely affected by the flavonoids (Sharpe et al 2002). From our perspective, however, the main question that arises is, If these chemicals were once present in our diet all year round for millions of developmental years, what effect has their loss had on us? Perhaps this testosterone surge would have been ameliorated.

Another group of plant biochemicals, the beta-carbolines, not only inhibits the action of steroids but also elevates neurotransmitter activity. Beta-carbolines, as well as occurring in some fruit and leaves, are also endogenously produced in the pineal gland of animals. If taken orally large doses of these chemicals can even be hallucinogenic.

Within the body beta-carbolines act as neuromodulators, fine-tuning the actions of neurotransmitters. They do this by preventing MAO

from breaking down the neurotransmitters serotonin and noradrenaline. The beta-carboline action can thus result in a buildup of these neurotransmitters at the synapses (the junctions of nerves), which allows greater neural activity. Indeed, this is just how hallucinogens work.

There is one specific beta-carboline (6-methoxy-1,2,3,4-tetrahydro-beta-carboline) that shares some of the properties of melatonin. Like melatonin, it shows a circadian rhythm within the body, it inhibits the development of the genital organs, and in females it can even interrupt the estrus cycle. It is also produced in the pineal gland and has now been given the much more accessible name of pinoline. Pinoline is a very effective antioxidant, it is particularly good at free-radical scavenging in brain tissue, and it can also act as a very safe antidepressant. It does not have the side effects associated with Prozac and other serotonin-based drugs and works by increasing serotonin turnover and recycling other essential neurotransmitters.

The harmala alkaloids are an extremely interesting group of beta-carbolines. Chemically they are very closely related to those in pinoline. They are found in the South American vine *Banisteriopsis caapi,* which is traditionally used in conjunction with a number of plants containing dimethyltryptamine (DMT) by tribal shamans to induce visions (see more on DMT in chapter 5). The specific alkaloid that is the active ingredient in the *Banisteriopsis* brew known as ayahuasca has even been given the name telepathine because of its profound properties. The same alkaloid also occurs in Assyrian rue (*Peganum harmala*), which is a plant with a very similar ancient healing and visionary pedigree. Passion flower (*Passiflora incarnata*), a common ingredient in herb teas, also contains these chemicals, but in weaker concentrations.

Fruits contain chemicals that are neurotransmitter precursors. These are chemicals that animals can use intact or that need little conversion to build neurotransmitters. They include plant hormones like indole-acetic acid and tryptophan. Tryptophan is a key amino acid that is found in protein-rich foods like meat, but it also occurs in some fruits like bananas and avocados. In Polynesia fruits rich in

tryptophan, like noni, have been traditionally used in healing, and tryptophan has even been used as the key ingredient in one type of sleeping pill. This amino acid is needed by the brain to make serotonin, and research has shown serotonin to be a body chemical of great importance. Its range of functions includes easing pain and tension and acting as a relaxant.

Fruits (as well as vegetables, nuts, seeds, and flowers) contain a whole host of other chemicals that while not being so powerful as beta-carbolines, will have some effect on the biochemistry of their consumers. Research has found that these substances have antibacterial, antifungal, antioxidant, anti-inflammatory, antimutagenic, and anti-allergenic properties, and they also can inhibit the activity of several enzymes. In experiments on mice, it has been found that many flavonoids inhibit the actions of MAO, and the potency of one, apigenin, was found to be comparable to that of clinically used MAO inhibitors (which are used to remedy human depression). Another flavonoid, quercetin, which occurs in nearly all plant foods and gives the color to, for example, apple skin, appears to have properties that reduce the risk of coronary heart disease and help to prevent ulcers, cataracts, allergies, and inflammation.

Dr. Richard Wurtman, a neuroendocrinologist at the Massachusetts Institute of Technology, spent years investigating neurotransmitters. After tracking the pathways they followed and studying their behavior and interactions, he concluded that the brain's ability to make certain neurotransmitters depends on the amount of nutrients circulating in the blood, and this is intimately influenced by what we eat. Fruit, therefore, as a rich source of these chemicals, can have a profound effect on our neural systems (Lieberman et al. 1985).

It is also of consequence that fruit is a rich source of simple sugars that do not need much alteration to make them useful to animal metabolism. They are easily converted to glucose—the number one brain fuel. This may be a factor of great importance. Fruit not only provides the chemicals to change brain activity but also the fuel to run it.

This short review of just a small fraction of plant chemicals serves to highlight their potency. Over an evolutionary timescale, a perpetual drip of these fruit chemicals via diet would have affected any specialist fruit-feeder. They represent a potentially powerful force for change. Flavonoids in particular are extremely potent endocrine modulators, and they would have been, in effect, an integral part of our ancestors' endocrine system for millions of years. Flavonoids powerfully inhibit both the activity of steroids and the conversion of androgens to estrogens. They also inhibit the action of the enzyme MAO (which takes the brakes off the body's production of melatonin). The fruit of the forest, via this linked complex of biochemical action, may have been just enough to initiate primate development and push this process forward toward the genesis of our own species.

THE FIRST PRIMATES

The primate story began during the Cretaceous period, some seventy million years ago, when small insect-eating mammals, which may have resembled the present-day tree shrews, climbed into a new, rich foliage to forage among the flowers, leaves, and fruit. Flowering trees were spreading across the globe, and the emergence of these plants brought a new level of complexity into the evolutionary equation. The more primitive plants, which came before, were not only less chemically rich but also disseminated their seeds without producing much in the way of fleshy fruits.

As with all living creatures, the DNA of this tree-climbing mammal would have dictated all aspects of its structure, from molecular, subcellular, cellular, and neural levels through to its gross anatomy and physiology. Similarly, its steroid hormones would have dictated the reading of the DNA codes. This is the standard biological model of life. Evolution runs on DNA variation, inheritance, and selection. But here is the key: Anything entering this relatively stable loop could have an effect (see figure 3.3).