Hormones and Sex
What’s Wrong with the Mamawawa?

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This chapter is about hormones and sex, a topic that some regard as unfit for conversation but that fascinates many others. Perhaps the topic of hormones and sex is so fascinating because we are intrigued by the fact that our sex is so greatly influenced by the secretions of a small pair of glands. Because we each think of our gender as fundamental and immutable, it is a bit disturbing to think that it could be altered with a few surgical snips and some hormone injections. And there is something intriguing about the idea that our sex lives might be enhanced by the application of a few hormones. For whatever reason, the topic of hormones and sex is always a hit with my students. Some remarkable things await you in this chapter; let’s go directly to them.

**Men-Are-Men-and-Women-Are-Women Assumption**

Many students bring a piece of excess baggage to the topic of hormones and sex: the men-are-men-and-women-are-women assumption—or “mamawawa.” This assumption is seductive; it seems so right that we are continually drawn to it without considering alternative views. Unfortunately, it is fundamentally flawed.

The men-are-men-and-women-are-women assumption is the tendency to think about femaleness and maleness as discrete, mutually exclusive, opposite categories. In thinking about hormones and sex, this general attitude leads one to assume that females have female sex hormones that give them female bodies and make them do “female” things, and that males have male sex hormones that give them male bodies and make them do opposite “male” things. Despite the fact that this approach to hormones and sex is inconsistent with the evidence, its simplicity, symmetry, and comfortable social implications draw us to it. That’s why this chapter grapples with it throughout. In so doing, this chapter encourages you to think about hormones and sex in new ways that are more consistent with the evidence.

### Developmental and Activational Effects of Sex Hormones

Before we begin discussing hormones and sex, you need to know that hormones influence sex in two fundamentally different ways (see Phoenix, 2008): (1) by influencing the development from conception to sexual maturity of the anatomical, physiological, and behavioral characteristics that distinguish one as female or male; and (2) by activating the reproduction-related behavior of sexually mature adults. Both the developmental (also called organizational) and activational effects of sex hormones are discussed in different sections of this chapter. Although the distinction between the developmental and activational effects of sex hormones is not always as clear as it was once assumed to be—for example, because the brain continues to develop into the late teens, adolescent hormone surges can have both effects—the distinction is still useful (Cohen-Bendahan, van de Beek, & Berenbaum, 2005).

### Neuroendocrine System

This section introduces the general principles of neuroendocrine function. It introduces these principles by focusing on the glands and hormones that are directly involved in sexual development and behavior.

The endocrine glands are illustrated in Figure 13.1. By convention, only the organs whose primary function appears to be the release of hormones are referred to as endocrine glands. However, other organs (e.g., the
stomach, liver, and intestine) and body fat also release hormones into general circulation (see Chapter 12), and they are thus, strictly speaking, also part of the endocrine system.

**Glands**

There are two types of glands: exocrine glands and endocrine glands. **Exocrine glands** (e.g., sweat glands) release their chemicals into ducts, which carry them to their targets, mostly on the surface of the body. **Endocrine glands** (ductless glands) release their chemicals, which are called hormones, directly into the circulatory system. Once released by an endocrine gland, a hormone travels via the circulatory system until it reaches the targets on which it normally exerts its effect (e.g., other endocrine glands or sites in the nervous system).

**Gonads**

Central to any discussion of hormones and sex are the **gonads**—the male **testes** (pronounced TEST-eez) and the female **ovaries** (see Figure 13.1). As you learned in Chapter 2, the primary function of the testes and ovaries is the production of **sperm cells** and **ova**, respectively. After **copulation** (sexual intercourse), a single sperm cell may **fertilize an ovum** to form one cell called a **zygote**, which contains all of the information necessary for the normal growth of a complete adult organism in its natural environment (see Primakoff & Myles, 2002). With the exception of ova and sperm cells, each cell of the human body has 23 pairs of chromosomes. In contrast, the ova and sperm cells contain only half that number, one member of each of the 23 pairs. Thus, when a sperm cell fertilizes an ovum, the resulting zygote ends up with the full complement of 23 pairs of chromosomes, one of each pair from the father and one of each pair from the mother.

Of particular interest in the context of this chapter is the pair of chromosomes called the **sex chromosomes**, so named because they contain the genetic programs that direct sexual development. The cells of females have two large sex chromosomes, called X chromosomes. In males, one sex chromosome is an X chromosome, and the other is called a Y chromosome. Consequently, the sex chromosome of every ovum is an X chromosome, whereas half the sperm cells have X chromosomes and half have Y chromosomes. Your sex with all its social, economic, and personal ramifications was determined by which of your father’s sperm cells won the dash to your mother’s ovum. If a sperm cell with an X sex chromosome won, you are a female; if one with a Y sex chromosome won, you are a male.

You might reasonably assume that X chromosomes are X-shaped and Y chromosomes are Y-shaped, but this is incorrect. Once a chromosome has duplicated, the two products remain joined at one point, producing an X shape. This is true of all chromosomes, including Y chromosomes. Because the Y chromosome is much smaller than the X chromosome, early investigators failed to discern one small arm and thus saw a Y. In humans, Y-chromosome genes encode only 27 proteins; in comparison, about 1,500 proteins are encoded by X-chromosome genes (see Arnold, 2004).

Writing this section reminded me of my seventh-grade basketball team, the “Nads.” The name puzzled our teacher because it was not at all like the names usually favored by pubescent boys—names such as the “Avengers,” the “Marauders,” and the “Vikings.” Her puzzlement ended abruptly at our first game as our fans began to chant their support. You guessed it: “Go Nads, Go! Go Nads, Go!” My 14-year-old spotted-faced teammates and I considered this to be humor of the most mature and sophisticated sort. The teacher didn’t.

**Classes of Hormones**

Vertebrate hormones fall into one of three classes: (1) amino acid derivatives, (2) peptides and proteins, and (3) steroids. **Amino acid derivative hormones** are hormones that are synthesized in a few simple steps from an amino acid molecule; an example is epinephrine, which is released from the **adrenal medulla** and synthesized from tyrosine. **Peptide hormones** and **protein hormones** are chains of amino acids—peptide hormones are short chains, and protein hormones are long chains. **Steroid hormones** are hormones that are synthesized from **cholesterol**, a type of fat molecule.

The hormones that influence sexual development and the activation of adult sexual behavior (i.e., the sex hormones) are all steroid hormones. Most other hormones produce their effects by binding to receptors in cell membranes. Steroid hormones can influence cells in this fashion; however, because they are small and fat-soluble, they can readily penetrate cell membranes and often affect cells in a second way. Once inside a cell, the steroid molecules can bind to receptors in the cytoplasm or nucleus and, by so doing, directly influence gene expression (amino acid derivative hormones and peptide hormones affect gene expression less commonly and by less direct mechanisms). Consequently, of all the hormones, steroid hormones tend to have the most diverse and long-lasting effects on cellular function (Brown, 1994).

**Sex Steroids**

The gonads do more than create sperm and egg cells; they also produce and release steroid hormones. Most people are surprised to learn that the testes and ovaries release the very same hormones. The two main classes of gonadal hormones are **androgens** and **estrogens**; **testosterone** is the most common androgen, and **estradiol** is the most common estrogen. The fact that adult ovaries tend to release more estrogens than they do androgens and that adult testes release more androgens than they do estrogens
has led to the common, but misleading, practice of referring to androgens as “the male sex hormones” and to estrogens as “the female sex hormones.” This practice should be avoided because of its men-are-men-and-women-are-women implication that androgens produce maleness and estrogens produce femaleness. They don’t.

The ovaries and testes also release a third class of steroid hormones called progestins. The most common progestin is progesterone, which in women prepares the uterus and the breasts for pregnancy. Its function in men is unclear.

Because the primary function of the adrenal cortex—the outer layer of the adrenal glands (see Figure 13.1)—is the regulation of glucose and salt levels in the blood, it is not generally thought of as a sex gland. However, in addition to its principal steroid hormones, it does release small amounts of all of the sex steroids that are released by the gonads.

Hormones of the Pituitary

The pituitary gland is frequently referred to as the master gland because most of its hormones are tropic hormones. Tropic hormones are hormones whose primary function is to influence the release of hormones from other glands (tropic means “able to stimulate or change something”). For example, gonadotropin is a pituitary tropic hormone that travels through the circulatory system to the gonads, where it stimulates the release of gonadal hormones.

The pituitary gland is really two glands, the posterior pituitary and the anterior pituitary, which fuse during the course of embryological development. The posterior pituitary develops from a small outgrowth of hypothalamic tissue that eventually comes to dangle from the hypothalamus on the end of the pituitary stalk (see Figure 13.2). In contrast, the anterior pituitary begins as part of the same embryonic tissue that eventually develops into the roof of the mouth; during the course of development, it pinches off and migrates upward to assume its position next to the posterior pituitary. It is the anterior pituitary that releases tropic hormones; thus, it is the anterior pituitary in particular, rather than the pituitary in general, that qualifies as the master gland.

Female Gonadal Hormone Levels Are Cyclic; Male Gonadal Hormone Levels Are Steady

Although men and women possess the same hormones, these hormones are not present at the same levels, and they do not necessarily perform the same functions. The major difference between the endocrine function of women and men is that in women the levels of gonadal and gonadotropic hormones go through a cycle that repeats itself every 28 days or so. It is these more-or-less regular hormone fluctuations that control the female menstrual cycle. In contrast, human males are, from a neuroendocrine perspective, rather dull creatures; males’ levels of gonadal and gonadotropic hormones change little from day to day.

Because the anterior pituitary is the master gland, many early scientists assumed that an inherent difference between the male and female anterior pituitary was the basis for the difference in male and female patterns of gonadotropic and gonadal hormone release. However, this hypothesis was discounted by a series of clever transplant studies conducted by Geoffrey Harris in the 1950s (see Raisman, 1997). In these studies, a cycling pituitary removed from a mature female rat became a steady-state pituitary when transplanted at the appropriate site in a male, and a steady-state pituitary removed from a mature male rat began to cycle once transplanted into a female. What these studies established was that anterior pituitaries are not inherently female (cyclical) or male (steady-state); their patterns
of hormone release are controlled by some other part of the body. The master gland seemed to have its own master. Where was it?

**Neural Control of the Pituitary**

The nervous system was implicated in the control of the anterior pituitary by behavioral research on birds and other animals that breed only during a specific time of the year. It was found that the seasonal variations in the light–dark cycle triggered many of the breeding-related changes in hormone release. If the lighting conditions under which the animals lived were reversed, for example, by having the animals transported across the equator, the breeding seasons were also reversed. Somehow, visual input to the nervous system was controlling the release of tropic hormones from the anterior pituitary.

The search for the particular neural structure that controlled the anterior pituitary turned, naturally enough, to the hypothalamus, the structure from which the pituitary is suspended. Hypothalamic stimulation and lesion experiments quickly established that the hypothalamus is the regulator of the anterior pituitary, but how the hypothalamus carries out this role remained a mystery. You see, the anterior pituitary, unlike the posterior pituitary, receives no neural input whatsoever from the hypothalamus, or from any other neural structure (see Figure 13.3).

**Control of the Anterior and Posterior Pituitary by the Hypothalamus**

There are two different mechanisms by which the hypothalamus controls the pituitary: one for the posterior pituitary and one for the anterior pituitary. The two major hormones of the posterior pituitary, vasopressin and oxytocin, are peptide hormones that are synthesized in the cell bodies of neurons in the paraventricular nuclei and supraoptic nuclei on each side of the hypothalamus (see Figure 13.3 and Appendix VI). They are then transported along the axons of these neurons to their terminals in the posterior pituitary and are stored there until the arrival of action potentials causes them to be released into the bloodstream. (Neurons that release hormones into general circulation are called neurosecretory cells.) Oxytocin stimulates contractions of the uterus during labor and the ejection of milk during suckling. Vasopressin (also called antidiuretic hormone) facilitates the reabsorption of water by the kidneys.

The means by which the hypothalamus controls the release of hormones from the neuron-free anterior pituitary was more difficult to explain. Harris (1955) suggested that the release of hormones from the anterior pituitary was itself regulated by hormones released from the hypothalamus. Two findings provided early support for this hypothesis. The first was the discovery of a vascular network, the hypothalampituitary portal system, that seemed well suited to the task of carrying hormones from the hypothalamus to the anterior pituitary. As Figure 13.4 on page 332 illustrates, a network of hypothalamic capillaries feeds a bundle of portal veins that carries blood down the pituitary stalk into another network of capillaries in the anterior pituitary. (A portal vein is a vein that connects one capillary network with another.) The second finding was the discovery that cutting the portal veins of the pituitary stalk disrupts the release of anterior pituitary hormones until the damaged veins regenerate (Harris, 1955).

**Discovery of Hypothalamic Releasing Hormones**

It was hypothesized that the release of each anterior pituitary hormone is controlled by a different hypothalamic hormone. The hypothalamic hormones that were thought to stimulate the release of an anterior pituitary hormone were referred to as releasing hormones; those thought to inhibit the release of an anterior pituitary hormone were referred to as release-inhibiting factors.

Efforts to isolate the putative (hypothesized) hypothalamic releasing and inhibitory factors led to a major breakthrough in the late 1960s. Guillemin and his colleagues isolated thyrotropin-releasing hormone from...
the hypothalamus of sheep, and Schally and his colleagues isolated the same hormone from the hypothalamus of pigs. Thyrrotropin-releasing hormone triggers the release of thyrotropin from the anterior pituitary, which in turn stimulates the release of hormones from the thyroid gland. For their efforts, Guillemin and Schally were awarded Nobel Prizes in 1977.

Schally’s and Guillemin’s isolation of thyrotropin-releasing hormone confirmed that hypothalamic releasing hormones control the release of hormones from the anterior pituitary and thus provided the major impetus for the isolation and synthesis of several other releasing hormones. Of direct relevance to the study of sex hormones was the subsequent isolation of gonadotropin-releasing hormone by Schally and his group (Schally, Kastin, & Arimura, 1971). This releasing hormone stimulates the release of both of the anterior pituitary’s gonadotropins: follicle-stimulating hormone (FSH) and luteinizing hormone (LH). All hypothalamic releasing hormones, like all tropic hormones, have proven to be peptides.

Regulation of Hormone Levels

Hormone release is regulated by three different kinds of signals: signals from the nervous system, signals from hormones, and signals from nonhormonal chemicals in the blood.

Regulation by Neural Signals

All endocrine glands, with the exception of the anterior pituitary, are directly regulated by signals from the nervous system. Endocrine glands located in the brain (i.e., the pituitary and pineal glands) are regulated by cerebral neurons; those located outside the CNS are innervated by the autonomic nervous system—usually by both the sympathetic and parasympathetic branches, which often have opposite effects on hormone release.

The effects of experience on hormone release are usually mediated by signals from the nervous system. It is extremely important to remember that hormone release can be regulated by experience—for example, many species that breed only in the spring are often prepared for reproduction by the release of sex hormones triggered by the increasing daily duration of daylight. This means that an explanation of any behavioral phenomenon in terms of a hormonal mechanism does not necessarily rule out an explanation in terms of an experiential mechanism. Indeed, hormonal and experiential explanations may merely be different aspects of the same hypothetical mechanism.

Regulation by Hormonal Signals

The hormones themselves also influence hormone release. You have already learned, for example, that the tropic hormones of...
the anterior pituitary influence the release of hormones from their respective target glands. However, the regulation of endocrine function by the anterior pituitary is not a one-way street. Circulating hormones often provide feedback to the very structures that influence their release: the pituitary gland, the hypothalamus, and other sites in the brain. The function of most hormonal feedback is the maintenance of stable blood levels of the hormones. Thus, high gonadal hormone levels usually have effects on the hypothalamus and pituitary that decrease subsequent gonadal hormone release, and low levels usually have effects that increase hormone release.

**Regulation by Nonhormonal Chemicals** Circulating chemicals other than hormones can play a role in regulating hormone levels. Glucose, calcium, and sodium levels in the blood all influence the release of particular hormones. For example, you learned in Chapter 12 that increases in blood glucose increase the release of insulin from the pancreas, and insulin, in turn, reduces blood glucose levels.

**Pulsatile Hormone Release**

Hormones tend to be released in pulses (see Armstrong et al., 2009; Khadra & Li, 2006); they are discharged several times per day in large surges, which typically last no more than a few minutes. Hormone levels in the blood are regulated by changes in the frequency and duration of the hormone pulses. One consequence of pulsatile hormone release is that there are often large minute-to-minute fluctuations in the levels of circulating hormones (e.g., Kooolhaas, Schuurman, & Wierpkema, 1980). Accordingly, when the pattern of human male gonadal hormone release is referred to as “steady,” it means that there are no major systematic changes in circulating gonadal hormone levels from day to day, not that the levels never vary.

**Summary Model of Gonadal Endocrine Regulation**

Figure 13.5 is a summary model of the regulation of gonadal hormones. According to this model, the brain controls the release of gonadotropin-releasing hormone from the hypothalamus into the hypothalamo-pituitary portal system, which carries it to the anterior pituitary. In the anterior pituitary, the gonadotropin-releasing hormone stimulates the release of gonadotropin, which is carried by the circulatory system to the gonads. In response to the gonadotropin, the gonads release androgens, estrogens, and progestins, which feed back into the pituitary and hypothalamus to regulate subsequent gonadal hormone release.

Armed with this general perspective of neuroendocrine function, you are ready to consider how gonadal hormones direct sexual development and activate adult sexual behavior.
Sexual differentiation in mammals begins at fertilization with the production of one of two different kinds of zygotes: either one with an XX (female) pair of sex chromosomes or one with an XY (male) pair. It is the genetic information on the sex chromosomes that normally determines whether development will occur along female or male lines. But be cautious here: Do not fall into the seductive embrace of the men-are-men-and-women-are-women assumption. Do not begin by assuming that there are two mutually exclusive, opposite categories.

Thinking Creatively

Under the influence of the Y chromosome, the medulla of the primordial gonad develops into a testis. If no Y chromosome is present, the cortex of the primordial gonad develops into an ovary.

**Fetal Hormones and Development of Reproductive Organs**

**Gonads** Figure 13.6 illustrates the structure of the gonads as they appear 6 weeks after fertilization. Notice that at this stage of development, each fetus, regardless of its genetic sex, has the same pair of gonadal structures, called primordial gonads (primordial means “existing at the beginning”). Each primordial gonad has an outer covering, or cortex, which has the potential to develop into an ovary; and each has an internal core, or medulla, which has the potential to develop into a testis.

Six weeks after conception, the Sry gene on the Y chromosome of the male triggers the synthesis of Sry protein (see Arnold, 2004; Wu et al., 2009), and this protein causes the medulla of each primordial gonad to grow and to develop into a testis. There is no female counterpart of Sry protein; in the absence of Sry protein, the cortical cells of the primordial gonads automatically develop into ovaries. Accordingly, if Sry protein is injected into a genetic female fetus 6 weeks after conception, the result is a genetic female with testes; or if drugs that block the effects of Sry protein are injected into a male fetus, the result is a genetic male with ovaries. Such “mixed-sex” individuals expose in a dramatic fashion the weakness of mammawawa thinking (thinking of “male” and “female” as mutually exclusive, opposite categories).

**Internal Reproductive Ducts** Six weeks after fertilization, both males and females have two complete sets of reproductive ducts. They have a male Wolffian system, which has the capacity to develop into the male reproductive ducts (e.g., the seminal vesicles, which hold the fluid in which sperm cells are ejaculated; and the vas deferens, through which the sperm cells travel to the seminal vesicles). And they have a female Müllerian system, which has the capacity to develop into the female ducts (e.g., the uterus; the upper part of the vagina; and the fallopian tubes, through which ova travel from the ovaries to the uterus, where they can be fertilized).

In the third month of male fetal development, the testes secrete testosterone and the Müllerian-inhibiting substance. As Figure 13.7 illustrates, the testosterone stimulates the development of the Wolffian system, and the Müllerian-inhibiting substance causes the Müllerian system to degenerate and the testes to descend into the scrotum—the sac that holds the testes outside the body cavity. Because it is testosterone—not the sex chromosomes—that triggers Wolffian development, genetic females who are injected with testosterone during the appropriate fetal period develop male reproductive ducts along with their female ones.

The differentiation of the internal ducts of the female reproductive system (see Figure 13.7) is not under the control of ovarian hormones; the ovaries are almost completely inactive during fetal development. The development of the Müllerian system occurs in any fetus that is not exposed to testicular hormones during the critical fetal period. Accordingly, normal female fetuses, ovariectomized female fetuses, and orchidectomized male fetuses all develop female reproductive ducts (Jost, 1972). Ovariectomy is the removal of the ovaries, and orchidectomy is the removal of the testes.
At 6 weeks, all human fetuses have the antecedents of both male (Wolffian) and female (Müllerian) reproductive ducts.

Male (XY) Female (XX)
- Seminal vesicle
- Fallopian tube
- Uterus
- Ovary
- Testis
- Scrotum

Under the influence of testicular testosterone, the Wolffian system develops, and Müllerian-inhibiting substance causes the Müllerian system to degenerate.

In the absence of testosterone, the Müllerian system develops into female reproductive ducts, and the Wolffian system fails to develop.

**FIGURE 13.7** The development of the internal ducts of the male and female reproductive systems from the Wolffian and Müllerian systems, respectively.

(bipotential precursor and its subsequent differentiation are illustrated in Figure 13.8 on page 336.)

In the second month of pregnancy, the bipotential precursor of the external reproductive organs consists of four parts: the glans, the urethral folds, the lateral bodies, and the labioscrotal swellings. Then it begins to differentiate. The glans grows into the head of the penis in the male or the clitoris in the female; the urethral folds fuse in the male or enlarge to become the labia minora in the female; the lateral bodies form the shaft of the penis in the male or the hood of the clitoris in the female; and the labioscrotal swellings form the scrotum in the male or the labia majora in the female.

Like the development of the internal reproductive ducts, the development of the external genitals is controlled by the presence or absence of testosterone. If testosterone is present at the appropriate stage of fetal development, male external genitals develop from the bipotential precursor; if testosterone is not present, development of the external genitals proceeds along female lines.

**Puberty: Hormones and Development of Secondary Sex Characteristics**

During childhood, levels of circulating gonadal hormones are low, reproductive organs are immature, and males and females differ little in general appearance. This period of developmental quiescence ends abruptly with the onset of puberty—the transitional period between childhood and adulthood during which fertility is achieved, the adolescent growth spurt occurs, and the secondary sex characteristics develop. Secondary sex characteristics are those features other than the reproductive organs that distinguish sexually mature men and women. The body changes that occur during puberty are illustrated in Figure 13.9 on page 337.

Puberty is associated with an increase in the release of hormones by the anterior pituitary (see Grumbach, 2002). The increase in the release of growth hormone—the only anterior pituitary hormone that does not have a gland as its primary target—acts directly on bone and muscle tissue to produce the pubertal growth spurt. Increases in the release of gonadotropic hormone and adrenocorticotrophic hormone cause the gonads and adrenal cortex to increase their release of gonadal and adrenal hormones, which in turn initiate the maturation of the genitals and the development of secondary sex characteristics.

The general principle guiding normal pubertal sexual maturation is a simple one: In pubertal males, androgen levels are higher than estrogen levels, and masculinization is the result; in pubertal females, the estrogens predominate, and the result is feminization. Individuals castrated prior to puberty do not become sexually mature unless they receive replacement injections of androgens or estrogens.

But even during puberty, its only period of relevance, the men-are-men-and-women-are-women assumption stumbles badly. You see, androstenedione, an androgen...
that is released primarily by the adrenal cortex, is normally responsible for the growth of pubic hair and axillary hair (underarm hair) in females. It is hard to take seriously the practice of referring to androgens as “male hormones” when one of them is responsible for the development of the female pattern of pubic hair growth. The male pattern is a pyramid, and the female pattern is an inverted pyramid (see Figure 13.9).

Do you remember how old you were when you started to go through puberty? In most North American and European countries, puberty begins at about 10.5 years of age for girls and 11.5 years for boys. I am sure you would have been unhappy if you had not started puberty until you were 15 or 16, but this was the norm in North America and Europe just a century and a half ago. Presumably, this acceleration of puberty has resulted from improvements in dietary, medical, and socioeconomic conditions.

13.3 Hormones and Sexual Development of Brain and Behavior

Biopsychologists have been particularly interested in the effects of hormones on the sexual differentiation of the brain and the effects of brain differences on behavior. This section reveals how seminal studies conducted in the 1930s generated theories that have gradually morphed, under the influence of subsequent research, into our current views. But first, let’s take a quick look at the differences between male and female brains.

Sex Differences in the Brain

The brains of men and women may look the same on casual inspection, and it may be politically correct to believe that they are—but they are not. The brains of men tend to be about 15% larger than those of women, and many other anatomical differences between average male and female brains have been documented. There are statistically significant sex differences in the volumes of various nuclei and fiber tracts, in the numbers and types of neural and glial cells that compose various structures, and in the numbers and types of synapses that connect the cells in various structures. Sexual dimorphisms (male–female structural differences) of the brain are typically studied in nonhuman mammals, but many have also been documented in humans (see Arnold, 2003; Cahill, 2005, 2006; de Vries & Södersten, 2009).

Let’s begin with the first functional sex difference to be identified in mammalian brains. It set the stage for everything that followed.

First Discovery of a Sex Difference in Mammalian Brain Function

The first attempts to discover sex differences in the mammalian brain focused on the factors that control the development of the steady and cyclic patterns
of gonadotropin release in males and females, respectively. The seminal experiments were conducted by Pfeiffer in 1936. In his experiments, some neonatal rats (males and females) were gonadectomized and some were not, and some received gonad transplants (ovaries or testes) and some did not.

Remarkably, Pfeiffer found that gonadectomizing neonatal rats of either genetic sex caused them to develop into adults with the female cyclic pattern of gonadotropin release. In contrast, transplantation of testes into gonadectomized or intact female neonatal rats caused them to develop into adults with the steady male pattern of gonadotropin release. Transplantation of ovaries had no effect on the pattern of hormone release. Pfeiffer concluded that the female cyclic pattern of gonadotropin release develops unless the preprogrammed female cyclicity is overridden by testosterone during perinatal development (see Harris & Levine, 1965).

Pfeiffer incorrectly concluded that the presence or absence of testicular hormones in neonatal rats influenced the development of the pituitary because he was not
aware of something we know today: The release of gonadotropins from the anterior pituitary is controlled by the hypothalamus. Once this was discovered, it became apparent that Pfeiffer’s experiments had provided the first evidence of the role of perinatal (around the time of birth) androgens in overriding the preprogrammed cyclic female pattern of gonadotropin release from the hypothalamus and initiating the development of the steady male pattern. This 1960s modification of Pfeiffer’s theory of brain differentiation to include the hypothalamus was consistent with the facts of brain differentiation as understood at that time, but subsequent research necessitated major revisions. The first of these major revisions became known as the aromatization hypothesis.

**Aromatization Hypothesis** What is aromatization? All gonadal and adrenal sex hormones are steroid hormones, and because all steroid hormones are derived from cholesterol, they have similar structures and are readily converted from one to the other. For example, a slight change to the testosterone molecule that occurs under the influence of the enzyme (a protein that influences a biochemical reaction without participating in it) aromatase converts testosterone to estradiol. This process is called aromatization (see Balthazart & Ball, 1998).

According to the **aromatization hypothesis**, perinatal testosterone does not directly masculinize the brain; the brain is masculinized by estradiol that has been aromatized from perinatal testosterone. Although the idea that estradiol—the alleged female hormone—masculinizes the brain may seem counterintuitive, there is strong evidence for it. Most of the evidence is of two types, both coming from experiments on rats and mice: (1) findings demonstrating masculinizing effects on the brain of early estradiol injections, and (2) findings showing that masculinization of the brain does not occur in response to testosterone that is administered with agents that block aromatization or in response to androgens that cannot be aromatized (e.g., dihydrotestosterone).

How do genetic females of species whose brains are masculinized by estradiol keep from being masculinized by their mothers’ estradiol, which circulates through the fetal blood supply? Alpha fetoprotein is the answer. **Alpha fetoprotein** is present in the blood of rats during the perinatal period, and it deactivates circulating estradiol by binding to it (Bakker et al., 2006; Bakker & Baum, 2007; De Mees et al., 2006). How, then, does estradiol masculinize the brain of the male fetus in the presence of the deactivating effects of alpha fetoprotein? Because testosterone is immune to alpha fetoprotein, it can travel unaffected from the testes to the brain cells where it is converted to estradiol. Estradiol is not broken down in the brain because alpha fetoprotein does not readily penetrate the blood–brain barrier.

**Modern Perspectives on Sexual Differentiation of Mammalian Brains** The view that the female program is the default program of brain development and is normally overridden in genetic males by perinatal exposure to testosterone aromatized to estradiol remained the preeminent theory of the sexual differentiation of the brain as long as research focused on the rat hypothalamus. Once studies of brain differentiation began to include other parts of the brain and other species, it became apparent that no single mechanism can account for the development of sexual dimorphisms of mammalian brains. The following findings have been particularly influential in shaping current views:

- Various sexual differences in brain structure and function have been found to develop by different mechanisms; for example, aromatase is found in only a few areas of the rat brain (e.g., the hypothalamus), and it is only in these areas that aromatization is critical for testosterone’s masculinizing effects (see Ball & Balthazart, 2006; Balthazart & Ball, 2006).
- Sexual differences in the brain have been found to develop by different mechanisms in different mammalian species (see McCarthy, Wright, & Schwartz, 2009); for example, aromatization plays a less prominent role in primates than in rats and mice (see Zuloaga et al., 2008).
- Various sex differences in the brain have been found to develop at different stages of development (Bakker & Baum, 2007); for example, many differences do not develop until puberty (Ahmed et al., 2008; Sisk & Zehr, 2005), a possibility ignored by early theories.
- Sex chromosomes have been found to influence brain development independent of their effect on hormones (Arnold, 2009; Jazon & Cahill, 2010); for example, different patterns of gene expression exist in the brains of male and female mice before the gonads become functional (Dewing et al., 2003).
- Although the female program of brain development had been thought to proceed normally in the absence of gonadal steroids, recent evidence suggests that estradiol plays an active role; knockout mice without the gene that forms estradiol receptors do not display a normal female pattern of brain development (see Bakker & Baum, 2007).

In short, there is overwhelming evidence that various sexual differences in mammalian brains emerge at different stages of development under different genetic and hormonal influences (see Wagner, 2006). Although the conventional view that a female program of development is the default does an excellent job of explaining differentiation of the reproductive organs, it falters badly when it comes to differentiation of the brain.

In studying the many sexual differences of mammalian brains, it is easy to lose sight of the main point: We still do...
not understand how any of the anatomical differences that have been identified influence behavior.

**Perinatal Hormones and Behavioral Development**

In view of the fact that perinatal hormones influence the development of the brain, it should come as no surprise that they also influence the development of behavior. Much of the research on perinatal hormones and behavioral development was conducted before the discoveries about brain development that we have just considered. Consequently, most of the studies have been based on the idea of a female default program that can be overridden by testosterone and have assessed the effects of perinatal testosterone exposure on reproductive behaviors in laboratory animals.

Phoenix and colleagues (1959) were among the first to demonstrate that the perinatal injection of testosterone masculinizes and defeminizes a genetic female’s adult copulatory behavior. First, they injected pregnant guinea pigs with testosterone. Then, when the litters were born, the researchers ovariec-tomized the female offspring. Finally, when these ovariec-tomized female guinea pigs reached maturity, the researchers injected them with testosterone and assessed their copulatory behavior. Phoenix and his colleagues found that the females that had been exposed to perinatal testosterone displayed more male-like mounting behavior in response to testosterone injections in adulthood than did adult females that had not been exposed to perinatal testosterone. And when, as adults, the female guinea pigs were injected with progesterone and estradiol and mounted by males, they displayed less lordosis—the intromission-facilitating arched-back posture that signals female receptivity.

In a study complementary to that of Phoenix and colleagues, Grady, Phoenix, and Young (1965) found that the lack of early exposure of male rats to testosterone both feminizes and demasculinizes their copulatory behavior as adults. Male rats castrated shortly after birth failed to display the normal male copulatory pattern of mounting, intromission (penis insertion), and ejaculation (ejection of sperm) when they were treated with testosterone and given access to a sexually receptive female; and when they were injected with estrogen and progesterone as adults, they exhibited more lordosis than did uncastrated controls.

The aromatization of perinatal testosterone to estradiol seems to be important for both the defeminization and the masculinization of rodent copulatory behavior (Goy & McEwen, 1980; Shapiro, Levine, & Adler, 1980). In contrast, that aromatization does not seem to be critical for these effects in monkeys (Wallen, 2005).

When it comes to the effects of perinatal testosterone on behavioral development, timing is critical. The ability of single injections of testosterone to masculinize and defeminize the rat brain seems to be restricted to the first 11 days after birth.

Because much of the research on hormones and behavioral development has focused on the copulatory act, we know less about the role of hormones in the development of receptive behaviors (solicitation behaviors) and in the development of gender-related behaviors that are not directly related to reproduction. However, perinatal testosterone has been reported to disrupt the receptive hopping, darting, and ear wiggling of receptive female rats; to increase the aggressiveness of female mice; to disrupt the maternal behavior of female rats; and to increase rough social play in female monkeys and rats.

Ethical considerations prohibit experimental studies of the developmental effects of hormones on human development. However, there have been many correlational studies of clinical cases and of ostensibly healthy individuals who received abnormal prenatal exposure to androgens (due to their own pathology or to drugs taken by their mothers). The results have been far from impressive. Cohen-Bendahan, van de Beek, and Berenbaum (2005) reviewed the extensive research literature and concluded that, despite many inconsistencies, the weight of evidence indicated that prenatal androgen exposure contributes to the differences in interests, spatial ability, and aggressiveness typically observed between men and women. However, there was no convincing evidence that differences in prenatal androgen exposure contribute to behavioral differences observed among women or among men.

Before you finish this subsection, I want to clarify an important point. If you are like many of my students, you may be wondering why biopsychologists who study the development of male–female behavioral differences always measure masculinization separately from defeminization and feminization separately from demasculinization. If you think that masculinization and defeminization are the same thing and that feminization and demasculinization are the same thing, you have likely fallen into the trap of the men-are-men-and-women-are-women assumption—that is, into the trap of thinking of maleness and femaleness as discrete, mutually exclusive, opposite categories. In fact, male behaviors and female behaviors can co-exist in the same individual, and they do not necessarily change in opposite directions if the individual receives physiological treatment such as hormones or brain lesions. For example, “male” behaviors (e.g., mounting receptive females) have been observed in the females of many different mammalian species, and “female” behaviors (e.g., lordosis) have been observed in males (see Dulac & Kimchi, 2007). And, lesions in medial preoptic areas have been shown to abolish male reproductive behaviors in both male and female rats, without affecting female behaviors (Singer, 1968). Think about this idea carefully, it plays an important role in later sections of the chapter.
present them. My main reason is expressed by a proverb: The exception proves the rule. Most people think this proverb means that the exception “proves” the rule in the sense that it establishes its truth, but this is clearly wrong: The truth of a rule is challenged by, not confirmed by, exceptions to it. The word proof comes from the Latin probare, which means “to test”—as in proving ground or printer’s proof—and this is the sense in which it is used in the proverb. Hence, the proverb means that the explanation of exceptional cases is a major challenge for any theory.

So far in this chapter, you have learned the “rules” according to which hormones seem to influence normal sexual development. Now, three exceptional cases are offered to prove (to test) these rules.

### The Case of Anne S., the Woman Who Wasn’t

Anne S., an attractive 26-year-old female, sought treatment for two sex-related disorders: lack of menstruation and pain during sexual intercourse (Jones & Park, 1971). She sought help because she and her husband of 4 years had been trying without success to have children, and she correctly surmised that her lack of a menstrual cycle was part of the problem.

A physical examination revealed that Anne was a healthy young woman. Her only readily apparent peculiarity was the sparseness and fineness of her pubic and axillary hair. Examination of her external genitals revealed no abnormalities; however, there were some problems with her internal genitals. Her vagina was only 4 centimeters long, and her uterus was underdeveloped.

At the start of this chapter, I said that you would encounter some remarkable things, and the diagnosis of Anne’s case certainly qualifies as one of them. Anne’s doctors concluded that her sex chromosomes were those of a man. No, this is not a misprint; they concluded that Anne, the attractive young housewife, had the genes of a genetic male. Three lines of evidence supported their diagnosis. First, analysis of cells scraped from the inside of Anne’s mouth revealed that they were of the male XY type. Second, a tiny incision in Anne’s abdomen, which enabled Anne’s physicians to look inside, revealed a pair of internalized testes but no ovaries. Finally, hormone tests revealed that Anne’s hormone levels were those of a male.

Anne suffers from complete androgenic insensitivity syndrome; all her symptoms stem from a mutation to the androgen receptor gene that rendered her androgen receptors totally unresponsive (see Fink et al., 1999; Goldstein, 2000). Complete androgen insensitivity is rare, occurring in about 5 of 100,000 male births.

During development, Anne’s testes released normal amounts of androgens for a male, but her body could not respond to them because of the mutation to her androgen...
receptor gene; and thus, her development proceeded as if no androgens had been released. Her external genitals, her brain, and her behavior developed along female lines, without the effects of androgens to override the female program, and her testes could not descend from her body cavity with no scrotum for them to descend into. Furthermore, Anne did not develop normal internal female reproductive ducts because, like other genetic males, her testes released Müllerian-inhibiting substance; that is why her vagina was short and her uterus undeveloped. At puberty, Anne’s testes released enough estrogens to feminize her body in the absence of the counteracting effects of androgens; however, adrenal androstenedione was not able to stimulate the growth of pubic and axillary hair.

Although the samples are small, patients with complete androgen insensitivity have been found to be comparable to genetic females. All aspects of their behavior that have been studied—including gender identity, sexual orientation, interests, and cognitive abilities—have been found to be typically female (see Cohen-Bendahan, van de Beek, & Berenbaum, 2005).

An interesting issue of medical ethics is raised by the androgenic insensitivity syndrome. Many people believe that physicians should always disclose all relevant findings to their patients. If you were Anne’s physician, would you tell her that she is a genetic male? Would you tell her husband? Her doctor did not. Anne’s vagina was surgically enlarged, she was counseled to consider adoption, and, as far as I know, she is still happily married and unaware of her genetic sex. On the other hand, I have heard from several women who suffer from partial androgenic insensitivity, and they recommended full disclosure. They had faced a variety of sexual ambiguities throughout their lives, and learning the cause helped them.

Elaine suffered from adrenogenital syndrome, which is the most common disorder of sexual development, affecting about 1 in 10,000. Adrenogenital syndrome is caused by congenital adrenal hyperplasia—a congenital deficiency in the release of the hormone cortisol from the adrenal cortex, which results in compensatory adrenal hyperactivity and the excessive release of adrenal androgens. This has little effect on the development of males, other than accelerating the onset of puberty, but it has major effects on the development of genetic females. Females who suffer from the adrenogenital syndrome are usually born with an enlarged clitoris and partially fused labia. Their gonads and internal ducts are usually normal because the adrenal androgens are released too late to stimulate the development of the Wolffian system.

Most female cases of adrenogenital syndrome are diagnosed at birth. In such cases, the abnormalities of the external genitals are immediately corrected, and cortisol is administered to reduce the levels of circulating adrenal androgens. Following early treatment, adrenogenital females grow up to be physically normal except that the onset of menstruation is likely to be later than normal. This makes them good subjects for studies of the effects of fetal androgen exposure on psychosexual development.

Adrenogenital teenage girls who have received early treatment tend to display more tomboyishness, greater strength, and more aggression than most teenage girls, and they tend to prefer boys’ clothes and toys, play mainly with boys, and daydream about future careers rather than motherhood (e.g., Collaer et al., 2008; Hines, 2003; Matthews et al., 2009). However, it is important not to lose sight of the fact that many teenage girls display similar characteristics—and why not? Accordingly, the behavior of treated adrenogenital females, although tending toward the masculine, is usually within the range considered to be normal female behavior by the current standards of our culture.

The most interesting questions about the development of females with adrenogenital syndrome concern their romantic and sexual preferences as adults. They seem to lag behind normal females in dating and marriage—perhaps because of the delayed onset of their menstrual cycle. Most are heterosexual, although a few studies have found an increased tendency for these women to express interest in bisexuality or homosexuality and a tendency to be less involved in heterosexual relationships (see Gooren, 2006). Complicating the situation further is the fact that these slight differences may not be direct consequences of early androgen exposure but arise from the fact that some adrenogenital girls have ambiguous genitalia and other male characteristics (e.g., body hair), which may result in different experiential influences.

Prior to the development of cortisol therapy in 1950, genetic females with adrenogenital syndrome were left untreated. Some were raised as boys and some as girls, but...
the direction of their pubertal development was unpredictable. In some cases, adrenal androgens predominated and masculinized their bodies; in others, ovarian estrogens predominated and feminized their bodies. Thus, some who were raised as boys were transformed at puberty into women and some who were raised as girls were transformed into men, with devastating emotional consequences.

The Case of the Twin Who Lost His Penis

One of the most famous cases in the literature on sexual development is that of a male identical twin whose penis was accidentally destroyed during circumcision at the age of 7 months. Because there was no satisfactory way of surgically replacing the lost penis, a respected expert in such matters, John Money, recommended that the boy be castrated, that an artificial vagina be created, that the boy be raised as a girl, and that estrogen be administered at puberty to feminize the body. After a great deal of consideration and anguish, the parents followed Money’s advice.

Money’s (1975) report of this case of ablation of the penis has been influential. It has been seen by some as the ultimate test of the nature–nurture controversy (see Chapter 2) with respect to the development of sexual identity and behavior. It seemed to pit the masculinizing effects of male genes and male prenatal hormones against the effects of being reared as a female. And the availability of a genetically identical control subject, the twin brother, made the case all the more interesting. According to Money, the outcome of this case strongly supported the social-learning theory of sexual identity. Money reported in 1975, when the patient was 12, that “she” had developed as a normal female, thus confirming his prediction that being gonadectomized, having the genitals surgically altered, and being raised as a girl would override the masculinizing effects of male genes and early androgens.

A long-term follow-up study published by impartial experts tells an entirely different story (Diamond & Sigmundson, 1997). Despite having female genitalia and being treated as a female, John/Joan developed along male lines. Apparently, the organ that determines the course of psychosocial development is the brain, not the genitals (Reiner, 1997). The following paraphrases from Diamond and Sigmundson’s report give you a glimpse of John/Joan’s life:

From a very early age, Joan tended to act in a masculine way. She preferred boys’ activities and games and displayed little interest in dolls, sewing, or other conventional female activities. When she was four, she was watching her father shave and her mother put on lipstick, and she began to put shaving cream on her face. When she was told to put makeup on like her mother, she said, “No, I don’t want no makeup, I want to shave.”

“Things happened very early. As a child, I began to see that I felt different about a lot of things than I was supposed to. I suspected I was a boy from the second grade on.”

Despite the absence of a penis, Joan often tried to urinate while standing, and she would sometimes go to the boys’ lavatory.

Joan was attractive as a girl, but as soon as she moved or talked her masculinity became apparent. She was teased incessantly by the other girls, and she often retaliated violently, which resulted in her expulsion from school.

Joan was put on an estrogen regimen at the age of 12 but rebelled against it. She did not want to feminize; she hated her developing breasts and refused to wear a bra.

At 14, Joan decided to live as a male and switched to John. At that time, John’s father tearfully revealed John’s entire early history to him. “All of a sudden everything clicked. For the first time I understood who and what I was.”

John requested androgen treatment, a mastectomy (surgical removal of breasts), and phaloplasty (surgical creation of a penis). He became a handsome and popular young man. He married at the age of 25 and adopted his wife’s children. He is strictly heterosexual.

John’s ability to ejaculate and experience orgasm returned following his androgen treatments. However, his early castration permanently eliminated his reproductive capacity.

“John” remained bitter about his early treatment and his inability to produce offspring. To save others from his experience, he cooperated in writing his biography, As Nature Made Him (Colapinto, 2000). His real name was David Reimer (see Figure 13.10). David never recovered from his emotional scars. On May 4, 2004, he committed suicide.

David Reimer’s case suggests that the clinical practice of surgically modifying a person’s sex at birth should be curtailed. Any such irrevocable treatments should await early puberty and the emergence of the patient’s sexual identity and sexual attraction. At that stage, a compatible course of treatment can be selected.

Do the Exceptional Cases Prove the Rule?

Do current theories of hormones and sexual development pass the test of the three preceding cases of exceptional sexual development? In my view, the answer is “yes.” Although current theories do not supply all of the answers, especially when it comes to brain dimorphisms and behavior, they have contributed greatly to the understanding of exceptional patterns of sexual differentiation of the body.
For centuries, cases of abnormal sexual development have baffled scholars, but now, armed with a basic understanding of the role of hormones in sexual development, they have been able to make sense of some of the most puzzling of such cases. Moreover, the study of sexual development has pointed the way to effective treatments. Judge these contributions for yourself by comparing your current understanding of these three cases with the understanding that you would have had if you had encountered them before beginning this chapter.

Notice one more thing about the three cases: Each of the three subjects was male in some respects and female in others. Accordingly, each case is a serious challenge to the men-are-men-and-women-are-women assumption: Male and female are not opposite, mutually exclusive categories.

13.5 Effects of Gonadal Hormones on Adults

Once an individual reaches sexual maturity, gonadal hormones begin to play a role in activating reproductive behavior. These activational effects are the focus of the first two parts of this section. They deal with the role of hormones in activating the reproduction-related behavior of men and women, respectively. The third part of this section deals with anabolic steroids, and the fourth describes the neuroprotective effects of estradiol.

Male Reproduction-Related Behavior and Testosterone

The important role played by gonadal hormones in the activation of male sexual behavior is clearly demonstrated by the asexualizing effects of orchidectomy. Bremer (1959) reviewed the cases of 157 orchidectomized Norwegians. Many had committed sex-related offenses and had agreed to castration to reduce the length of their prison terms.

Two important generalizations can be drawn from Bremer’s study. The first is that orchidectomy leads to a reduction in sexual interest and behavior; the second is that the rate and the degree of the loss are variable. About half the men became completely asexual within a few weeks of the operation; others quickly lost their ability to achieve an erection but continued to experience some sexual interest and pleasure; and a few continued to copulate successfully, although somewhat less enthusiastically, for the duration of the study. There were also body changes: a reduction of hair on the trunk, extremities, and face; the deposition of fat on the hips and chest; a softening of the skin; and a reduction in strength.

Of the 102 sex offenders in Bremer’s study, only 3 were reconvicted of sex offenses. Accordingly, he recommended castration as an effective treatment of last resort for male sex offenders.

Why do some men remain sexually active for months after orchidectomy, despite the fact that testicular hormones are cleared from their bodies within days? It has been suggested that adrenal androgens may play some role in the maintenance of sexual activity in some castrated men, but there is no direct evidence for this hypothesis.

Orchidectomy removes, in one fell swoop—or, to put it more precisely, in two fell swoops—a pair of glands that release many hormones. Because testosterone is the major testicular hormone, the major symptoms of orchidectomy have been generally attributed to the loss of testosterone, rather than to the loss of some other testicular hormone or to some nonhormonal consequence of the surgery. The therapeutic effects of replacement injections of testosterone have confirmed this assumption.

The Case of the Man Who Lost and Regained His Manhood

The very first case report of the effects of testosterone replacement therapy concerned an unfortunate 38-year-old World War I veteran, who was castrated in 1918 at the age of 19 by a shell fragment that removed his testes but left his penis undamaged.
His body was soft; it was as if he had almost no muscles at all; his hips had grown wider and his shoulders seemed narrower than when he was a soldier. He had very little drive... 

Just the same this veteran had married, in 1924, and you’d wonder why, because the doctors had told him he would surely be impotent [unable to achieve an erection]. . . . he made some attempts at sexual intercourse “for his wife’s satisfaction” but he confessed that he had been unable to satisfy her at all. . . .

Dr. Foss began injecting it [testosterone] into the feeble muscles of the castrated man. . . .

After the fifth injection, erections were rapid and prolonged. . . . But that wasn’t all. During twelve weeks of treatment he had gained eighteen pounds, and all his clothes had become too small. . . . testosterone had restored a broken man to a manhood he had lost forever. (de Kruif, 1945, pp. 97–100)

Since this first clinical trial, testosterone has breathed sexuality into the lives of many men. Testosterone does not, however, eliminate the sterility (inability to reproduce) of males who lack functional testes.

The fact that testosterone is necessary for male sexual behavior has led to two widespread assumptions: (1) that the level of a man’s sexuality is a function of the amount of testosterone he has in his blood, and (2) that a man’s sex drive can be increased by increasing his testosterone levels. Both assumptions are incorrect. Sex drive and testosterone levels are uncorrelated in healthy men, and testosterone injections do not increase their sex drive.

It seems that each healthy male has far more testosterone than is required to activate the neural circuits that produce his sexual behavior and that having more than the minimum is of no advantage in this respect (Sherwin, 1988). A classic experiment by Grunt and Young (1952) clearly illustrates this point.

First, Grunt and Young rated the sexual behavior of each of the male guinea pigs in their experiment. Then, on the basis of the ratings, the researchers divided the male guinea pigs into three experimental groups: low, medium, and high sex drive. Following castration, the sexual behavior of all of the guinea pigs fell to negligible levels within a few weeks (see Figure 13.11), but it recovered after the initiation of a series of testosterone replacement injections. The important point is that although each subject received the same, very large replacement injections of testosterone, the injections simply returned each to its previous level of copulatory activity. The conclusion is clear: With respect to the effects of testosterone on sexual behavior, more is not necessarily better.

Dihydrotestosterone, a nonaromatizable androgen, restores the copulatory behavior of castrated male primates (e.g., Davidson, Kwan, & Greenleaf, 1982); however, it fails to restore the copulatory behavior of castrated male rodents (see MacLusky & Naftolin, 1981). These findings indicate that the restoration of copulatory behavior by testosterone occurs by different mechanisms in rodents and primates: It appears to be a direct effect of testosterone in primates, but appears to be produced by estradiol aromatized from testosterone in rodents (see Ball & Balthazart, 2006).

**Female Reproduction-Related Behavior and Gonadal Hormones**

Sexually mature female rats and guinea pigs display 4-day cycles of gonadal hormone release. There is a gradual increase in the secretion of estrogens by the developing follicle (ovarian structure in which eggs mature) in the
2 days prior to ovulation, followed by a sudden surge in progesterone as the egg is released. These surges of estradiol and progesterone initiate estrus—a period of 12 to 18 hours during which the female is fertile, receptive (likely to assume the lordosis posture when mounted), proceptive (likely to engage in behaviors that serve to attract the male), and sexually attractive (smelling of chemicals that attract males).

The close relation between the cycle of hormone release and the estrous cycle—the cycle of sexual receptivity—in female rats and guinea pigs and in many other mammalian species suggests that female sexual behavior in these species is under hormonal control. The effects of ovariectomy confirm this conclusion; ovariectomy of female rats and guinea pigs produces a rapid decline of both proceptive and receptive behaviors. Furthermore, estrus can be induced in ovariectomized rats and guinea pigs by an injection of estradiol followed about a day and a half later by an injection of progesterone.

Women are different from female rats, guinea pigs, and other mammals when it comes to the hormonal control of their sexual behavior: Female primates are the only female mammals that are motivated to copulate during periods of nonfertility (Ziegler, 2007). Moreover, ovariectomy has surprisingly little direct effect on either their sexual motivation or their sexual behavior (e.g., Martin, Roberts, & Clayton, 1980). Other than sterility, the major consequence of ovariectomy in women is a decrease in vaginal lubrication.

Numerous studies have investigated the role of estradiol in the sex drive of women by relating various measures of their sexual interest and activity to phases of their menstrual cycles. The results of this research are difficult to interpret. Some women do report that their sex drive is related to their menstrual cycles, and many studies have reported statistically significant correlations. The confusion arises because many studies have found no significant correlations, and because many different patterns of correction have been reported (see Regan, 1996; Sanders & Bancroft, 1982). No single pattern has emerged that characterizes fluctuations in human female sexual motivation. Paradoxically, there is evidence that the sex drive of women is under the control of androgens (the so-called male sex hormones), not estrogens (see Davis & Tran, 2001; Sherwin, 1988). Apparently, enough androgens are released from the human adrenal glands to maintain the sexual motivation of women even after their ovaries have been removed. Support for the theory that androgens control human female sexuality has come from three sources:

- In experiments with nonhuman female primates, replacement injections of testosterone, but not estradiol, increased the proceptivity of ovariectomized and adrenalectomized rhesus monkeys (see Everitt & Herbert, 1972; Everitt, Herbert, & Hamer, 1971).

- In correlational studies of healthy women, various measures of sexual motivation have been shown to correlate with testosterone levels but not with estradiol levels (see Bancroft et al., 1983; Morris et al., 1987).

- In clinical studies of women following ovariectomy and adrenalectomy or menopause, replacement injections of testosterone, but not of estradiol, rekindled the patients’ sexual motivation (see de Paula et al., 2007; Sherwin, Gelfand, & Brender, 1985).

This research has led to the development of a testosterone skin patch for the treatment of low sex drive in women. The patch has been shown to be effective for women who have lost their sex drive following radical hysterectomy (Buster et al., 2005), Although a few studies have reported positive correlations between blood testosterone levels and the strength of sex drive in women (e.g., Turna et al., 2004), most women with low sex drive do not have low blood levels of testosterone (Davis et al., 2005; Gerber et al., 2005). Thus, the testosterone skin patch is unlikely to help most women with libido problems.

Although neither the sexual motivation nor the sexual activity of women has found to be linked to their menstrual cycles, the type of men they prefer may be. Several studies have shown that women prefer masculine faces more on their fertile days than on their nonfertile days (e.g., Gangestad, Thornhill, & Garver-Apgar, 2005; Penton-Voak & Perrett, 2000).

### Anabolic Steroid Abuse

Anabolic steroids are steroids, such as testosterone, that have anabolic (growth-promoting) effects. Testosterone itself is not very useful as an anabolic drug because it is broken down soon after injection and because it has undesirable side effects. Chemists have managed to synthesize a number of potent anabolic steroids that are long-acting, but they have not managed to synthesize one that does not have side effects.

According some experts, we are currently in the midst of an epidemic of anabolic steroid abuse. Many competitive athletes and bodybuilders are self-administering appallingly large doses, and many others use them for cosmetic purposes. Because steroids are illegal, estimates of the numbers who use them are likely underestimates. Still, the results of some surveys have been disturbing: For example, a survey by the U.S. Centers for Disease Control and Prevention (Eaton et al., 2005) found that almost 5% of high school students had been steroid users.

### Effects of Anabolic Steroids on Athletic Performance

Do anabolic steroids really increase the muscularity and strength of the athletes who use them? Surprisingly, the
early scientific evidence was inconsistent (see Yesalis & Bahrke, 1995), even though many athletes and coaches believe that it is impossible to compete successfully at the highest levels of their sports without an anabolic steroid boost. The failure of the early experiments to confirm the benefits that had been experienced by many athletes likely results from two shortcomings of the research. First, the early experimental studies tended to use doses of steroids smaller than those used by athletes and for shorter periods of time. Second, the early studies were often conducted on volunteers who were not involved in intense training. However, despite the inconsistent experimental evidence, the results achieved by numerous individual steroid users, such as the man pictured in Figure 13.12, are convincing.

**Physiological Effects of Anabolic Steroids**

There is general agreement (see Maravelias et al., 2005; Yesalis & Bahrke, 1995) that people who take high doses of anabolic steroids risk side effects. In men, the negative feedback from high levels of anabolic steroids reduces gonadotropin release; this leads to a reduction in testicular activity, which can result in *testicular atrophy* (wasting away of the testes) and sterility. *Gynecomastia* (breast growth in men) can also occur, presumably as the result of the aromatization of anabolic steroids to estrogens.

In women, anabolic steroids can produce *amenorrhea* (cessation of menstruation), *sterility*, *hirsutism* (excessive growth of body hair), growth of the clitoris, development of a masculine body shape, baldness, shrinking of the breasts, and deepening and coarsening of the voice. Unfortunately, some of the masculinizing effects of anabolic steroids on women appear to be irreversible.

Both men and women who use anabolic steroids can suffer muscle spasms, muscle pains, blood in the urine, acne, general swelling from the retention of water, bleeding of the tongue, nausea, vomiting, and a variety of psychotic behaviors, including fits of depression and anger (Maravelias et al., 2005). Oral anabolic steroids produce cancerous liver tumors.

One controlled evaluation of the effects of exposure to anabolic steroids was conducted in adult male mice. Adult male mice were exposed for 6 months to a cocktail of four anabolic steroids at relative levels comparable to those used by human athletes (Bronson & Matherne, 1997). None of the mice died during the period of steroid exposure; however, by 20 months of age (6 months after termination of the steroid exposure), 52% of the steroid-exposed mice had died, whereas only 12% of the controls had died.

There are two general points of concern about the adverse health consequences of anabolic steroids: First, the use of anabolic steroids in puberty, before developmental programs of sexual differentiation are complete, is particularly risky (see Farrell & McGinnis, 2003). Second, many of the adverse effects of anabolic steroids may take years to be manifested—steroid users who experience few immediate adverse effects may pay the price later.

**Behavioral Effects of Anabolic Steroids**

Other than those focusing on athletic performance, which you have just read about, few studies have systematically investigated the effects of anabolic steroids on behavior. However, because of the similarity between anabolic steroids and testosterone, there has been some suggestion that anabolic steroid use might increase aggressive and sexual behaviors. Let’s take a brief look at the evidence.

Evidence that anabolic steroid use increases aggression comes almost entirely from the claims of steroid users. These anecdotal reports are unconvincing for three reasons:

- Because of the general belief that testosterone causes aggression, reports of aggressive behavior in male steroid users might be a consequence of expectation.
- Many individuals who use steroids (e.g., professional fighters or football players) are likely to have been aggressive before they started treatment.
- Aggressive behavior might be an indirect consequence of increased size and masculinity.
In one experimental assessment of the effects of anabolic steroids on aggression, Pope, Kouri, and Hudson (2000) administered either testosterone or placebo injections in a double-blind study of 53 men. Each volunteer completed tests of aggression and kept a daily aggression-related diary. Pope and colleagues found increases in aggression in only a few of the volunteers.

Although their similarity to testosterone suggests that steroids might increase sexual motivation, there is no evidence of such an effect. On the contrary, there are several anecdotal reports of the disruptive effects of anabolic steroids on human male copulatory behavior, and controlled experiments have shown that anabolic steroids disrupt the copulatory behavior of both male and female rodents (see Clark & Henderson, 2003).

Neuroprotective Effects of Estradiol

Although estradiol is best known for its sex-related organizational and activational effects, this hormone also can reduce the brain damage associated with stroke and various neurodegenerative disorders (see De Butte-Smith et al., 2009). For example, Yang and colleagues (2003) showed that estradiol administered to rats just before, during, or just after the induction of cerebral hypoxia (reduction of oxygen to the brain) reduced subsequent brain damage (see Chapter 10).

Estradiol has been shown to have several neurotrophic effects that might account for its neuroprotective properties (see Chapter 10). It has been shown to reduce inflammation, encourage axonal regeneration, promote synaptogenesis (see Stein & Hoffman, 2003; Zhang et al., 2004), and increase adult neurogenesis (see Chapter 10). Injection of estradiol initially increases the number of new neurons created in the dentate gyri of the hippocampuses of adult female rats and then, about 48 hours later, there is a period of reduced neurogenesis (see Galea et al., 2006; Ormerod, Falconer, & Galea, 2003). As well as increasing adult neurogenesis, estradiol increases the survival rate of the new neurons (see Galea et al., 2006; Ormerod & Galea, 2001b).

The discovery of estradiol’s neuroprotective properties has created a lot of excitement among neuroscientists. These properties may account for women’s greater longevity and their lower incidence of several common neuropsychological disorders, such as Parkinson’s disease. They may also explain the decline in memory and some other cognitive deficits experienced by postmenopausal women (see Bisagno, Bowman, & Luine, 2003; Gandy, 2003).

Several studies have assessed the ability of estrogen treatments to reduce the cognitive deficits experienced by postmenopausal women. The results of some studies have been encouraging, but others have observed either no benefit or an increase in cognitive deficits (see Blaustein, 2008; Frick, 2009). Two suggestions have been made for improving the effectiveness of estradiol therapy: First, Sherwin (2007) pointed out that such therapy appears to be effective in both humans and nonhumans only if the estradiol treatment is commenced at menopause or shortly thereafter. Second, Marriott and Wenk (2004) argued that the chronically high doses that have been administered to postmenopausal women are unnatural and potentially toxic; they recommend instead that estradiol therapy should mimic the natural cycle of estradiol levels in premenopausal women.
Neural Mechanisms of Sexual Behavior

Major differences among cultures in sexual practices and preferences indicate that the control of human sexual behavior involves the highest levels of the nervous system (e.g., association cortex), and this point is reinforced by controlled demonstrations of the major role played by experience in the sexual behaviors of nonhuman animals (see Woodson, 2002; Woodson & Balleine, 2002; Woodson, Balleine, & Gorski, 2002). Nevertheless, research on the neural mechanisms of sexual behavior has focused almost exclusively on hypothalamic circuits. Consequently, I am forced to do the same here: When it comes to the study of the neural regulation of sexual behavior, the hypothalamus is virtually the only game in town.

Why has research on the neural mechanisms of sexual behavior focused almost exclusively on hypothalamic circuits? There are three obvious reasons: First, because of the difficulty of studying the neural mechanisms of complex human sexual behaviors, researchers have focused on the relatively simple, controllable copulatory behaviors (e.g., ejaculation, mounting, and lordosis) of laboratory animals (see Agmo & Ellingsen, 2003), which tend to be controlled by the hypothalamus. Second, because the hypothalamus controls gonadotropin release, it was the obvious place to look for sexually dimorphic structures and circuits that might control copulation. And third, early studies confirmed that the hypothalamus does play a major role in sexual behavior, and this finding led subsequent neuroscientific research on sexual behavior to focus on that brain structure.

Structural Differences between the Male and Female Hypothalamus

You have already learned that the male hypothalamus and the female hypothalamus are functionally different in their control of anterior pituitary hormones (steady versus cyclic release, respectively). In the 1970s, structural differences between the male and female hypothalamus were discovered in rats (Raisman & Field, 1971). Most notably, Gorski and his colleagues (1978) discovered a nucleus in the medial preoptic area of the rat hypothalamus that was several times larger in males (see Figure 13.13). They called this nucleus the sexually dimorphic nucleus.

At birth, the sexually dimorphic nuclei of male and female rats are the same size. In the first few days after birth, the male sexually dimorphic nuclei grow at a high rate and the female sexually dimorphic nuclei do not. The growth of the male sexually dimorphic nuclei is normally triggered by estradiol, which has been aromatized from testosterone (see McEwen, 1987). Accordingly, castrating day-old

FIGURE 13.13 Nissl-stained coronal sections through the preoptic area of male and female rats. The sexually dimorphic nuclei are larger in male rats than in female rats. (Based on Gorski et al., 1978.)
(but not 4-day-old) male rats significantly reduces the size of their sexually dimorphic nuclei as adults, whereas injecting neonatal (newborn) female rats with testosterone significantly increases the size of theirs (Gorski, 1980)—see Figure 13.14. Although the overall size of the sexually dimorphic nucleus diminishes only slightly in male rats that are castrated in adulthood, specific areas of the nucleus do display significant degeneration (Bloch & Gorski, 1988).

The size of a male rat’s sexually dimorphic nucleus is correlated with the rat’s testosterone levels and aspects of its sexual activity (Anderson et al., 1986). However, bilateral lesions of the sexually dimorphic nucleus have only slight disruptive effects on male rat sexual behavior (e.g., De Jonge et al., 1989; Turkenburg et al., 1988), and the specific function of this nucleus is unclear.

Since the discovery of the sexually dimorphic nuclei in rats, other sex differences in hypothalamic anatomy have been identified in rats and in other species (see Swaab & Hofman, 1995; Witelson, 1991). In humans, for example, there are nuclei in the preoptic (Swaab & Fliers, 1985), suprachiasmatic (Swaab et al., 1994), and anterior (Allen et al., 1989) regions of the hypothalamus that differ in men and women.

**Hypothalamus and Male Sexual Behavior**

The medial preoptic area (which includes the sexually dimorphic nucleus) is one area of the hypothalamus that plays a key role in male sexual behavior (see Dominguez & Hull, 2005). Destruction of the entire area abolishes sexual behavior in the males of all mammalian species that have been studied (see Hull et al., 1999). In contrast, medial preoptic area lesions do not eliminate the female sexual behaviors of females, but they do eliminate the male sexual behaviors (e.g., mounting) that are often observed in females (Singer, 1968). Thus, bilateral medial preoptic lesions appear to abolish male copulatory behavior in both sexes. Conversely, electrical stimulation of the medial preoptic area elicits copulatory behavior in male rats (Malsbury, 1971; Rodriguez-Manzo et al., 2000), and copulatory behavior can be reinstated in castrated male rats by medial preoptic implants of testosterone (Davidson, 1980).

The medial preoptic circuits that control male sexual behavior appear to be dopaminergic (see Dominguez & Hull, 2005; Lagoda et al., 2004). Dopamine agonists microinjected into the medial preoptic area facilitate male sexual behavior, whereas dopamine agonists block it.

It is not clear why males with medial preoptic lesions stop copulating. One possibility is that the lesions disrupt the ability of males to copulate; another is that the lesions reduce the motivation of the males to engage in sexual behavior. The evidence is mixed, but it favors the hypothesis that the medial preoptic area is involved in the motivational aspects of male sexual behavior (Paredes, 2003).

The medial preoptic area appears to control male sexual behavior via a tract that projects to an area of the midbrain called the lateral tegmental field. Destruction of this tract disrupts the sexual behavior of male rats (Brackett & Edwards, 1984). Moreover, the activity of individual neurons in the lateral tegmental field of male rats is often correlated with aspects of the copulatory act (Shimura & Shimokochi, 1990); for example, some neurons in the lateral tegmental field fire at a high rate only during intromission.

**Hypothalamus and Female Sexual Behavior**

The ventromedial nucleus (VMN) of the rat hypothalamus contains circuits that appear to be critical for female sexual behavior. Female rats with bilateral lesions of the
VMN do not display lordosis, and they are likely to attack suitors who become too ardent.

You have already learned that an injection of progesterone brings into estrus an ovariectomized female rat that received an injection of estradiol about 36 hours before. Because the progesterone by itself does not induce estrus, the estradiol must in some way prime the nervous system so that the progesterone can exert its effect. This priming effect appears to be mediated by the large increase in the number of progesterone receptors that occurs in the VMN and surrounding area following an estradiol injection (Blaustein et al., 1988); the estradiol exerts this effect by entering VMN cells and influencing gene expression. Confirming the role of the VMN in estrus is the fact that microinjections of estradiol and progesterone directly into the VMN induce estrus in ovariectomized female rats (Pleim & Barfield, 1988).

The influence of the VMN on the sexual behavior of female rats appears to be mediated by a tract that descends to the periaqueductal gray (PAG) of the tegmentum. Destruction of this tract eliminates female sexual behavior (Hennessey et al., 1990), as do lesions of the PAG itself (Sakuma & Pfaff, 1979).

In conclusion, although many parts of the brain play a role in sexual behavior, much of the research has focused on the role of the hypothalamus in the copulatory behavior of rats. Several areas of the hypothalamus influence this copulatory behavior, and several hypothalamic nuclei are sexually dimorphic in rats, but the medial preoptic area and the ventromedial nucleus are two of the most widely studied. Male rat sexual behavior is influenced by a tract that runs from the medial preoptic area to the lateral tegmental field, and female rat sexual behavior is influenced by a tract that runs from the ventromedial nucleus to the periaqueductal gray (see Figure 13.15).

Sexual Orientation and Genes

Research has shown that differences in sexual orientation have a genetic basis. For example, Bailey and Pillard (1991) studied a group of male homosexuals who had twin brothers, and they found that 52% of the monozygotic twin brothers and 22% of the dizygotic twin brothers were homosexual. In a comparable study of female twins by the same group of researchers (Bailey et al., 1993), the concordance rates for homosexuality were 48% for monozygotic twins and 16% for dizygotic twins.

Considerable excitement was created by the claim that a gene for male homosexuality had been localized on one end of the X chromosome (Hamer et al., 1993). However, subsequent research has not confirmed this claim (see Mustanski, Chivers, & Bailey, 2002; Rahman, 2005).

Sexual Orientation and Early Hormones

Many people mistakenly assume that homosexuals have lower levels of sex hormones. They don’t: Heterosexuals and homosexuals do not differ in their levels of circulating hormones. Moreover, orchidectomy reduces the sexual behavior of both heterosexual and homosexual males, but it

13.7
Sexual Orientation and Sexual Identity

So far, this chapter has not addressed the topic of sexual orientation. As you know, some people are heterosexual (sexually attracted to members of the other sex), some are homosexual (sexually attracted to members of the same sex), and some are bisexual (sexually attracted to members of both sexes). Also, the chapter has not addressed the topic of sexual identity (the sex, male or female, that a person believes himself or herself to be). A discussion of sexual orientation and sexual identity is a fitting conclusion to this chapter because it brings together the exception-proves-the-rule and anti-mamawawa themes.
does not redirect it; and replacement injections simply reactivate the preferences that existed prior to surgery.

Many people also assume that sexual preference is a matter of choice. It isn’t: People discover their sexual preferences; they don’t choose them. Sexual preferences seem to develop very early, and a child’s first indication of the direction of sexual attraction usually does not change as he or she matures. Could perinatal hormone exposure be the early event that shapes sexual orientation?

Because experiments involving levels of perinatal hormone exposure are not feasible with humans, efforts to determine whether perinatal hormone levels influence the development of sexual orientation have focused on nonhuman species. A consistent pattern of findings has emerged. In those species that have been studied (e.g., rats, hamsters, ferrets, pigs, zebra finches, and dogs), it has not been uncommon to see males engaging in female sexual behavior, being mounted by other males; nor has it been uncommon to see females engaging in male sexual behavior, mounting other females. However, because the defining feature of sexual orientation is sexual preference, the key studies have examined the effect of early hormone exposure on the sex of preferred sexual partners. In general, the perinatal castration of males has increased their preference as adults for male sex partners; similarly, prenatal testosterone exposure in females has increased their preference as adults for female sex partners (see Baum et al., 1990; Henley, Nunez, & Clemens, 2009; Hrabovsky & Hutson, 2002).

On the one hand, we need to exercise prudence in drawing conclusions about the development of sexual preferences in humans based on the results of experiments on laboratory species; it would be a mistake to ignore the profound cognitive and emotional components of human sexuality, which have no counterpart in laboratory animals. On the other hand, it would also be a mistake to think that a pattern of results that runs so consistently through so many mammalian species has no relevance to humans (Swaab, 2004).

In addition, there are some indications that perinatal hormones do influence sexual orientation in humans—although the evidence is sparse (see Diamond, 2009). Support comes from the quasiexperimental study of Ehrhardt and her colleagues (1985). They interviewed adult women whose mothers had been exposed to diethylstilbestrol (a synthetic estrogen) during pregnancy. The women’s responses indicated that they were significantly more sexually attracted to women than was a group of matched controls. Ehrhardt and her colleagues concluded that perinatal estrogen exposure does encourage homosexuality and bisexuality in women but that its effect is relatively weak: The sexual behavior of all but 1 of the 30 participants was primarily heterosexual.

One promising line of research on sexual orientation focuses on the fraternal birth order effect, the finding that the probability of a man’s being homosexual increases as a function of the number of older brothers he has (Blanchard, 2004; Blanchard & Lippa, 2007). A recent study of blended families (families in which biologically related siblings were raised with adopted siblings or step-siblings) found that the effect is related to the number of boys previously born to the mother, not the number of boys one is reared with (Bogaert, 2007). The effect is quite large: The probability of a male’s being homosexual increases by 33.3% for every older brother he has (see Puts, Jordan, & Breedlove, 2006), and an estimated 15% of gay men can attribute their homosexuality to the fraternal birth order effect (Cantor et al., 2002). The maternal immune hypothesis has been proposed to explain the fraternal birth order effect; this hypothesis is that some mothers become progressively more immune to masculinizing hormones in male fetuses (see Blanchard, 2004), and a mother’s immune system might deactivate masculinizing hormones in her younger sons.

What Triggers the Development of Sexual Attraction?

The evidence indicates that most girls and boys living in Western countries experience their first feelings of sexual attraction at about 10 years of age, whether they are heterosexual or homosexual (see Quinsey, 2003). This finding is at odds with the usual assumption that sexual interest is triggered by puberty, which, as you have learned, currently tends to occur at 10.5 years of age in girls and at 11.5 years in boys.

McCintock and Herdt (1996) have suggested that the emergence of sexual attraction may be stimulated by adrenal cortex steroids. Unlike gonadal maturation, adrenal maturation occurs at about the age of 10.

Is There a Difference in the Brains of Homosexuals and Heterosexuals?

The brains of homosexuals and heterosexuals must differ in some way, but how? Many studies have attempted to identify neuroanatomical, neuropsychological, neurophysiological, and hormonal response differences between homosexuals and heterosexuals.

In a highly publicized study, LeVay (1991) found that the structure of one hypothalamic nucleus in male homosexuals was intermediate between that in female heterosexuals and that in male heterosexuals. This study has not been consistently replicated, however. Indeed, no reliable difference between the brains of heterosexuals and homosexuals has yet been discovered (see Rahman, 2005).

Sexual Identity

Sexual identity is the sex, male or female, that a person believes himself or herself to be. Usually, sexual identity coincides with a person’s anatomical sex, but not always.
Transsexualism is a condition of sexual identity in which an individual believes that he or she is trapped in a body of the other sex. To put it mildly, the transsexual faces a bizarre conflict: “I am a woman (or man) trapped in the body of a man (or woman). Help!” It is important to appreciate the desperation of these individuals; they do not merely think that life might be better if their gender were different. Although many transsexuals do seek surgical sexual reassignment (surgery to change their sex), the desperation is better indicated by how some of them dealt with their problem before surgical sexual reassignment was an option: Some biological males (psychological females) attempted self-castration, and others consumed copious quantities of estrogen-containing face creams in order to feminize their bodies.

How does surgical sexual reassignment work? I will describe the male-to-female procedure. The female-to-male procedure is much more complex (because a penis must be created) and far less satisfactory (for example, because a surgically created penis has no erectile potential), and male-to-female sexual reassignment is three times more prevalent.

The first step in male-to-female reassignment is psychiatric assessment to establish that the candidate for surgery is a true transsexual. Once accepted for surgical re-assignment, each transsexual receives in-depth counseling to prepare for the difficulties that will ensue. If the candidate is still interested in re-assignment after counseling, estrogen administration is initiated to feminize the body; the hormone regimen continues for life to maintain the changes. Then, comes the surgery. The penis and testes are surgically removed, and female external genitalia and a vagina are constructed—the vagina is lined with skin and nerves from the former penis so that it will have sensory nerve endings that will respond to sexual stimulation. Finally, some patients have cosmetic surgery to feminize the face (e.g., to reduce the size of the Adam’s apple). Generally, the adjustment of transsexuals after surgical sexual reassignment is good.

The causes of transsexualism are unknown. Transsexualism was once thought to be a product of social learning, that is, of inappropriate child-rearing practices (e.g., mothers dressing their little boys in dresses). The occasional case that is consistent with this view can be found, but in most cases, there is no obvious cause (see Diamond, 2009; Swaab, 2004). One of the major difficulties in identifying the causes and mechanisms of transsexualism is that there is no comparable syndrome in nonhumans (Baum, 2006).

Indepedence of Sexual Orientation and Sexual Identity

To complete this chapter, I would like to remind you of two of its main themes and show you how useful they are in thinking about one of the puzzles of human sexuality. One of the two themes is that the exception proves the rule: that a powerful test of any theory is its ability to explain exceptional cases. The second is that the mamawawa is seriously flawed: We have seen that men and women are similar in some ways (Hyde, 2005) and different in others (Cahill, 2006), but they are certainly not opposites, and their programs of development are neither parallel nor opposite.

Here, I want to focus on the puzzling fact that sexual attraction, sexual identity, and body type are sometimes unrelated. For example, consider transsexuals: They, by definition, have the body type of one sex and the sexual identity of the other sex, but the orientation of their sexual attraction is an independent matter. Some transsexuals with a male body type are sexually attracted to females, others are sexually attracted to males, and others are sexually attracted to neither—and this is not changed by sexual reassignment (see Van Goozen et al., 2002). Also, it is important to realize that a particular sex-related trait in an individual can lie at midpoint between the female and male norms.

Obviously, the mere existence of homosexuality and transsexualism is a challenge to the mamawawa, the assumption that males and females belong to distinct and opposite categories. Many people tend to think of “femaleness” and “maleness” as being at opposite ends of a continuum, with a few abnormal cases somewhere between the two. Perhaps this is how you tend to think. However, the fact that body type, sexual orientation, and sexual identity are often independent constitutes a serious attack on any assumption that femaleness and maleness lie at opposite ends of a single scale. Clearly, femaleness or maleness is a combination of many different attributes (e.g., body type, sexual orientation, and sexual identity), each of which can develop quite independently. This is a real puzzle for many people, including scientists, but what you have already learned in this chapter suggests a solution.

Think back to the section on brain differentiation. Until recently, it was assumed that the differentiation of the human brain into its usual female and male forms occurred through a single testosterone-based mechanism. However, a different notion has developed from recent evidence. Now, it is clear that male and female brains differ in many ways and that the differences develop at different times and by different mechanisms. If you keep this developmental principle in mind, you will have no difficulty understanding how it is possible for some individuals to be female in some ways and male in others, and to lie between the two norms in still others.

This analysis exemplifies a point I make many times in this book. The study of biopsychology often has important personal and social implications: The search for the neural basis of a behavior frequently provides us with a greater understanding of that behavior. I hope that you now have a greater understanding of, and acceptance of, differences in human sexuality.

Themes Revisited

Three of the book’s four major themes were repeatedly emphasized in this chapter: the evolutionary perspective, clinical implications, and thinking creatively themes.

The evolutionary perspective theme was pervasive. It received frequent attention because most experimental studies of hormones and sex have been conducted in nonhuman species. The other major source of information about hormones and sex has been the study of human clinical cases, which is why the clinical implications theme was prominent in the cases of the woman who wasn’t, the little girl who grew into a boy, the twin who lost his penis, and the man who lost and regained his manhood.

The thinking creatively theme was emphasized throughout the chapter because conventional ways of thinking about hormones and sex have often been at odds with the results of biopsychological research. If you are now better able to resist the seductive appeal of the men-are-men-and-women-are-women assumption, you are a more broadminded and understanding person than when you began this chapter. I hope you have gained an abiding appreciation of the fact that maleness and femaleness are multidimensional and, at times, ambiguous variations of each other.

The fourth major theme of the book, neuroplasticity, arose during the discussions of the effects of hormones on the development of sex differences in the brain and of the neurotrophic effects of estradiol.

Think about It

1. Over the last century and a half, the onset of puberty has changed from age 15 or 16 to age 10 or 11, but there has been no corresponding acceleration in psychological and intellectual development. Precocious puberty is like a loaded gun in the hand of a child. Discuss.
2. Do you think adult sex-change operations should be permitted? Should they be permitted in preadolescents? Explain and supply evidence.
3. What should be done about the current epidemic of anabolic steroid abuse? Would you make the same recommendation if a safe anabolic steroid were developed? If a safe drug that would dramatically improve your memory were developed, would you take it?
4. Heterosexuality cannot be understood without studying homosexuality. Discuss.
5. What treatment should be given to infants born with ambiguous external genitals? Why?
6. Sexual orientation, sexual identity, and body type are not always related. Discuss.

Key Terms

13.1 Neuroendocrine System
Exocrine glands (p. 329)
Endocrine glands (p. 329)
Hormones (p. 329)
Gonads (p. 329)
Testes (p. 329)
Ovaries (p. 329)
Copulation (p. 329)
Zygote (p. 329)
Sex chromosomes (p. 329)
Amino acid derivatives (p. 329)
Peptide hormones (p. 329)
Protein hormones (p. 329)
Steroid hormones (p. 329)
Androgens (p. 329)
Estrogens (p. 329)
Testosterone (p. 329)
Estradiol (p. 329)
Progesterins (p. 330)
Progesterone (p. 330)
Adrenal cortex (p. 330)
Gonadotropin (p. 330)
Posterior pituitary (p. 330)
Pituitary stalk (p. 330)
Anterior pituitary (p. 330)
Menstrual cycle (p. 330)
Vasopressin (p. 331)
Oxytocin (p. 331)
Paraventricular nuclei (p. 331)
Supraoptic nuclei (p. 331)

Hypothalamopituitary portal system (p. 331)
Releasing hormones (p. 331)
Release-inhibiting factors (p. 331)
Thyrotropin-releasing hormone (p. 331)
Thyrotropin (p. 332)
Gonadotropin-releasing hormone (p. 332)
Follicle-stimulating hormone (FSH) (p. 332)
Luteinizing hormone (LH) (p. 332)
Pulsatile hormone release (p. 333)

13.2 Hormones and Sexual Development of the Body
Sry gene (p. 334)
Sry protein (p. 334)
Wolffian system (p. 334)
Müllerian system (p. 334)
Müllerian-inhibiting substance (p. 334)
Scrotum (p. 334)
Ovariectomy (p. 334)
Orchidectomy (p. 334)
Gonadectomy (p. 335)
Genitals (p. 335)
Secondary sex characteristics (p. 335)
Growth hormone (p. 335)
13.3 Hormones and Sexual Development of Brain and Behavior

Aromatase (p. 338)
Aromatization (p. 338)
Aromatization hypothesis (p. 338)
Alpha fetoprotein (p. 338)
Masculinizes (p. 339)
Defeminizes (p. 339)
Lordosis (p. 339)

Feminizes (p. 339)
Demasculinizes (p. 339)
Intromission (p. 339)
Ejaculation (p. 339)
Proceptive behaviors (p. 339)

13.4 Three Cases of Exceptional Human Sexual Development

Androgenic insensitivity syndrome (p. 340)
Adrenogenital syndrome (p. 341)
Congenital adrenal hyperplasia (p. 341)
Ablatio penis (p. 342)

13.5 Effects of Gonadal Hormones on Adults

Replacement injections (p. 343)
Impotent (p. 344)
Estrus (p. 345)
Estrous cycle (p. 345)
Anabolic steroids (p. 345)

13.6 Neural Mechanisms of Sexual Behavior

Medial preoptic area (p. 348)
Sexually dimorphic nucleus (p. 348)
Ventromedial nucleus (VMN) (p. 349)

13.7 Sexual Orientation and Sexual Identity

Heterosexual (p. 350)
Homosexual (p. 350)
Bisexual (p. 350)
Sexual identity (p. 350)
Fraternal birth order effect (p. 351)
Maternal immune hypothesis (p. 351)
Transsexualism (p. 352)

Quick Review

Test your comprehension of the chapter with this brief practice test. You can find the answers to these questions as well as more practice tests, activities, and other study resources at www.mypsychlab.com.

1. The ovaries and testes are
   a. zygotes.
   b. exocrine glands.
   c. gonads.
   d. both a and c
   e. both b and c

2. Gonadotropin is released by the
   a. anterior pituitary.
   b. posterior pituitary.
   c. hypothalamus.
   d. gonads.
   e. adrenal cortex.

3. Releasing hormones are released by the
   a. anterior pituitary.
   b. posterior pituitary.
   c. hypothalamus.
   d. gonads.
   e. adrenal cortex.

4. Which term refers specifically to the surgical removal of the testes?
   a. orchidectomy
   b. castration
   c. gonadectomy
   d. ovariotomy
   e. both b and c

5. Adrenogenital syndrome typically has severe consequences for
   a. rodents but not primates.
   b. Caucasians but not other ethnic groups.
   c. girls but not boys.
   d. boys but not girls.
   e. men but not women.