CHAPTER

26

Sex Differences in Brain and Behavioral Development

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OUTLINE

26.1 INTRODUCTION

Psychological and neural sex differences are a topic of great interest for their relevance to both applied and basic science questions. From an applied perspective, they figure into discussions ranging from women's underrepresentation in science and math careers (Ceci and Williams, 2010; Halpern et al., 2007) to sex differences in incidences and forms of psychopathology (Hartung and Widiger, 1998; Zahn-Waxler et al., 2008). From a basic science perspective, sex represents an important dimension of individual difference, and factors that lead to differences between the sexes can help us to understand variation generally. The focus of this chapter is sex differences in the human brain and behavior, with an emphasis on cognitive abilities; our goal is to describe what is known and hypothesized about the differences, their development, and their etiology, and to begin to link brain differences to cognitive differences.

The chapter is organized into several sections. First, we summarize the evidence concerning psychological sex differences in human beings and the ways in which they develop across age, focusing on changes from infancy through young adulthood. Second, we consider the main theories that have been offered to explain the differences and the evidence that supports those perspectives. Third, we summarize the evidence concerning sex differences in the human brain and what (little) is known about their development. Fourth, we review the small body of research about the etiology and psychological correlates of brain sex differences. Fifth, we emphasize the gaps in our knowledge and provide suggestions for further research.

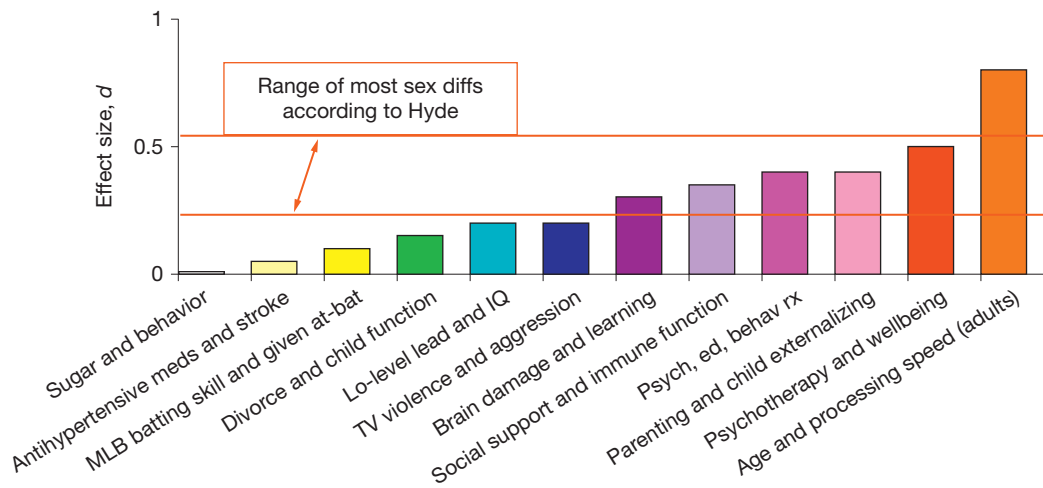## 26.2 PSYCHOLOGICAL SEX DIFFERENCES: NATURE AND DEVELOPMENT

Sex differences are found in many psychological domains, from sensory thresholds to career choices. We focus here on cognitive sex differences but note other significant psychological domains in which the sexes differ. Our goal is not to provide an exhaustive review of the extensive literature in this area, but to provide a summary of the findings, highlighting the key differences and, in later sections, explanations of these differences, as well as the links between cognitive and brain sex differences. Detailed reviews, with supporting references, are available elsewhere, as cited throughout the chapter. Consistent with others, we describe sex differences in terms of *effect size*, d (Cohen, 1988): small ($d \sim 0.2$, 85% overlap in distributions of the sexes), moderate ($d \sim 0.5$, 67% overlap, probably noticeable), and large ($d \sim 0.8$, 53% overlap, very noticeable).

As a prelude to a description of the differences, we note that there is some controversy over the size of these differences, whether they have declined over time, and whether they even exist (Hyde, 2005). Some of the controversy relates to what is a meaningful difference, with some arguing that sex differences are too small to be worthwhile. But sex differences are among the largest effects in psychology; compare the effects described below with typical effects in psychology and medicine described elsewhere (e.g., Meyer et al., 2001). This is illustrated in Figure 26.1. Furthermore, there is not always a perfect mapping between the size of a difference and its significance.

26.2.1 Cognitive Abilities

The sexes do not differ in overall intelligence (discussed in Camarata and Woodcock, 2006; Halpern, 2012; Roivainen, 2011), but, as detailed below, they do differ in their pattern of abilities: on average, boys and men are better than girls and women in spatial and some mathematical skills, whereas girls and women are better than boys and men in many verbal abilities, memory, and processing speed (Halpern, 2012). One analysis of the structure of intelligence (Johnson and Bouchard, 2007) concludes that it consists of three dimensions: a rotation–verbal dimension (at one end of the dimension, tasks measuring mental rotation and other spatial skills, and at the other end, verbal tasks); a focus–diffusion dimension (at one end, attention focused on one main stimulus in the environment, and at the other end, attention focused diffusely on several cues simultaneously); and memory. Typically, men were found

FIGURE 26.1 Psychological sex differences in behavior compared to other health and psychological effects, described in standard deviation units, *d*. (data from Hyde, 2005; Meyer et al., 2001)
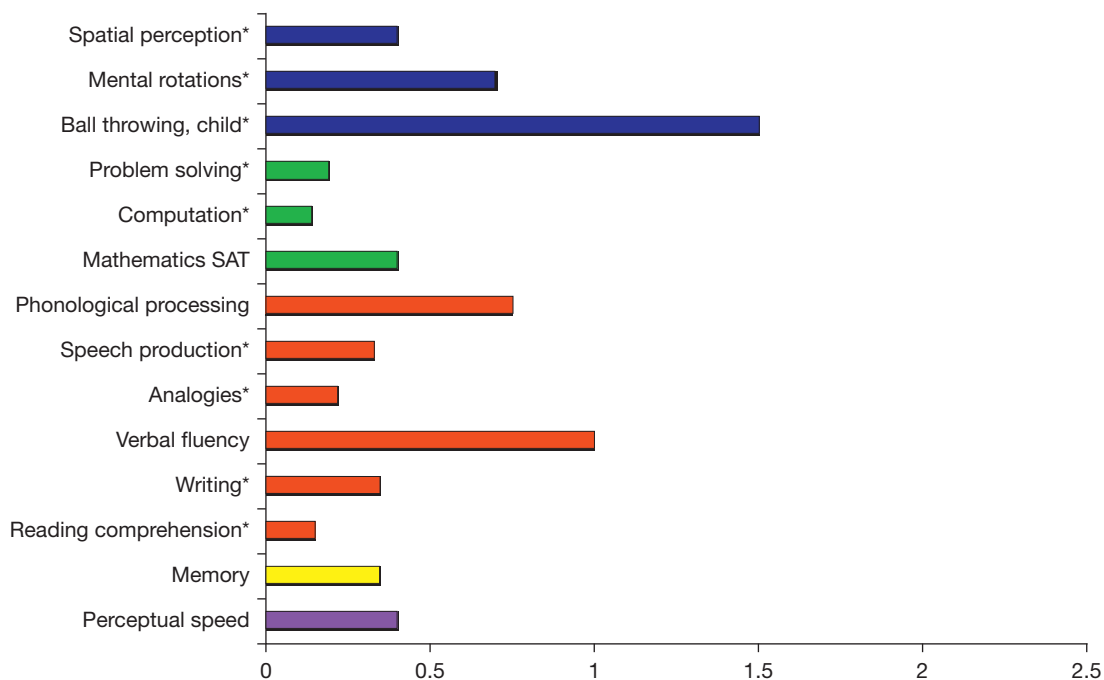
FIGURE 26.2 Sample sex differences in cognitive abilities: absolute value of the differences in standard deviation units, *d* (data from *Blakemore et al., 2009*); asterisks (*) indicate results from meta-analyses.

to be nearer the rotation and focus ends of those two dimensions, and women at the verbal and diffusion ends, and women to have better memory. Figure 26.2 provides a summary of the cognitive sex differences expressed in standard deviation units, *d*.

26.2.1.1 Spatial Abilities

One widely studied cognitive sex difference is spatial ability. There are several ways to parse the domain, but boys and men outperform girls and women in most aspects of spatial ability, with the size of the difference varying across abilities (Halpern, 2012; Lawton, 2010). The largest sex difference is in mental rotation, especially rotation of objects in three dimensions. This sex difference is apparent beginning in infancy (Moore and Johnson, 2008; Quinn and Liben, 2008), with boys and men having better ability than girls and women and with the difference increasing slightly from childhood to adulthood (Geiser et al., 2008).

There are moderately sized sex differences in spatial perception and the ability to identify spatial relations with respect to one's body in relation to external space

or to identify the true vertical or horizontal (Halpern, 2012). This ability is measured by tasks such as the 'rod and frame task' (Voyer and Bryden, 1993) and 'water level task' (Vasta and Liben, 1996).

There are also sex differences in abilities related to navigating in the real world (Lawton, 2010), an ability typically referred to as 'wayfinding.' Boys and men are better than girls and women at remembering and navigating to distant locations in large spaces; some of the difference results from sex differences in strategy, with men relying on cardinal (north, south, east, and west) directions and women relying on landmarks. Considering larger issues of the spatial environment, there is a huge sex disparity among National Geography Bee winners (despite equal participation from boys and girls); the sex ratio increases at each level of competition, so that in many years, all ten finalists are boys (Liben, 1995).

There is one aspect of spatial ability on which the sex difference is reversed: memory for spatial location. Girls and women are better than boys and men in remembering the location of objects (Voyer et al., 2007).

26.2.1.2 Mathematical Abilities

The sexes differ in quantitative abilities, with the differences again varying by type of ability and age (Halpern, 2012). In school, girls get better grades than do boys in arithmetic and mathematics classes (as they do in all classes), but they do not perform as well on standardized tests of math knowledge and skills (e.g., the SAT). The main math sex difference is in problem-solving tasks, with boys outperforming girls, especially at older ages. Recent data show the sex difference to be small (Lindberg et al., 2010), although the size of the difference is larger in some countries than in others, in ways that are sometimes, but not always, related to indices of gender equality in those countries (Else-Quest et al., 2010; Guiso et al., 2008). There are no sex differences in understanding mathematical concepts, and girls outperform boys in computation, especially before puberty.

The sexes also differ in their variability in spatial and mathematical abilities (Hedges and Nowell, 1995). For example, for the past 20 years, about four times as many seventh-grade boys as girls have scored in the high ranges of the SAT-Mathematics (Wai et al., 2010); before that time, there were even higher ratios of boys to girls at the top end.

26.2.1.3 Verbal Abilities

There are many different kinds of verbal and language-related skills, such as vocabulary size, use of correct grammar, reading, doing anagrams, and following verbal instructions. The sexes are similar on some skills. When there are differences, they are generally in the direction of girls and women having better skills than boys and men, although the size of the difference varies with ability and age (Halpern, 2012).

Language learning occurs earlier in girls than in boys, with boys catching up by age 6 (Bornstein et al., 2004; Wallentin, 2009). Language disorders are more common in boys than in girls (Wallentin, 2009). In terms of specific verbal skills, females have a small to moderate advantage over males in several skills, most prominently reading comprehension, verbal fluency, and phonological processing, but males have a small edge in analogies (Halpern, 2012). In terms of verbal abilities that are particularly important educationally, there is great concern about boys' lag in reading performance (Chudowsky and Chudowsky, 2010). Boys also write less well than girls, a difference that is especially notable at the highest ability levels (Hedges and Nowell, 1995; Wai et al., 2010).

Females also process verbal materials more rapidly than males, including intelligence scale subtests, verbal fluency tests asking for many words to be generated quickly, letters of the alphabet, and digits (Camarata and Woodcock, 2006; Roivainen, 2011). Females' faster processing speed may be one contributor to their superior reading and writing abilities.

26.2.1.4 Memory

As with other cognitive domains, there are several aspects of memory. In some, the sexes do not differ. But in several, girls and women are better than boys and men: they show more accurate recall for learning facts or material that they read, more readily learn lists of words, have better recall for lists of common objects such as animals, food, furniture, and appliances, and have better recognition memory (Halpern, 2012; Johnson and Bouchard, 2007). Women have better verbal memory in part because they use more efficient clustering strategies.

Sex differences in memory are especially consistent for episodic memory, that is, memory of specific events and episodes. For example, women are better than men at recognizing faces that they have seen before. Many episodic memories are verbally based, but women have better episodic memories even when the tasks are not verbal (e.g., face recognition) except when the memory tasks are clearly spatial, in which case men do better (Herlitz et al., 2010). Women also recall the identities and locations of objects better than men, although it has been suggested that this might be due to women's better memories overall (Voyer et al., 2007). Sex differences in memory are generally small to moderate in size.

26.2.1.5 Perceptual Speed

In addition to faster processing of verbally based cognitive tasks, girls and women are faster than boys and men in another type of speeded task, called perceptual

speed (Burns and Nettelbeck, 2005). Most intelligence tests have some subscales that measure this ability. In general, these tests involve the ability to perceive details and shift attention quickly, often while using fine motor skills such as finger movements (Halpern, 2012). The difference ranges from small to large, depending on the particular measure used.

26.2.2 Noncognitive Sex Differences

There are many other psychological domains in which the sexes differ, but we focus here on those that have received the most attention, that are relatively large in size, or that illustrate important points about studying sex differences (e.g., the importance of developmental status, measurement, and social context). Figure 26.3 provides a summary of the noncognitive sex differences expressed in standard deviation units, *d*.

26.2.2.1 Physical and Motor Skills

Sex differences in physical and motor skills vary by aspect and age (Blakemore et al., 2009). Boys are more active than girls (Eaton and Enns, 1986; Else-Quest et al., 2006), and activity level becomes increasingly sex-differentiated with age, with the differences largest in familiar, nonthreatening settings and when peers are present. There are few sex differences in early milestones of reaching, sitting, crawling, and walking, but differences in motor skills begin to appear in the second year (Mondschein et al., 2000). The earlier neurological development of girls compared to boys results in

early development of some abilities, such as eye–hand coordination. Overall, girls develop sooner than and are superior to boys with respect to fine motor skills, whereas boys have better gross motor skills and are stronger than girls (Largo et al., 2001a,b), which combine with boys' advantage in spatial skills to result in large sex differences in targeting (hitting a target with a ball) (Kimura, 1999). Sex differences in many (but not all) physical and motor abilities increase with age, although the patterns vary considerably depending on the particular skill (Dorfberger et al., 2009; Thomas and French, 1985).

26.2.2.2 Activity Interests

One of the largest and most important sex differences concerns interests (Blakemore et al., 2009; Ruble et al., 2006). In childhood, boys and girls prefer and engage with different toys (e.g., trucks and dolls) and participate in different activities (e.g., playing sports and playing dress-up). In adolescence, boys and girls continue to prefer and participate in different leisure activities (e.g., building things and dance), household chores (e.g., taking out the garbage and preparing food), and academic pursuits (e.g., math and language arts). In adulthood, men and women continue to prefer and participate in different activities, and are differentially represented in different occupations; for example, men prefer occupations that involve working with things, and women prefer occupations that involve working with people (Su et al., 2009). Although the sexes overlap in their interests and activity participation, the average differences
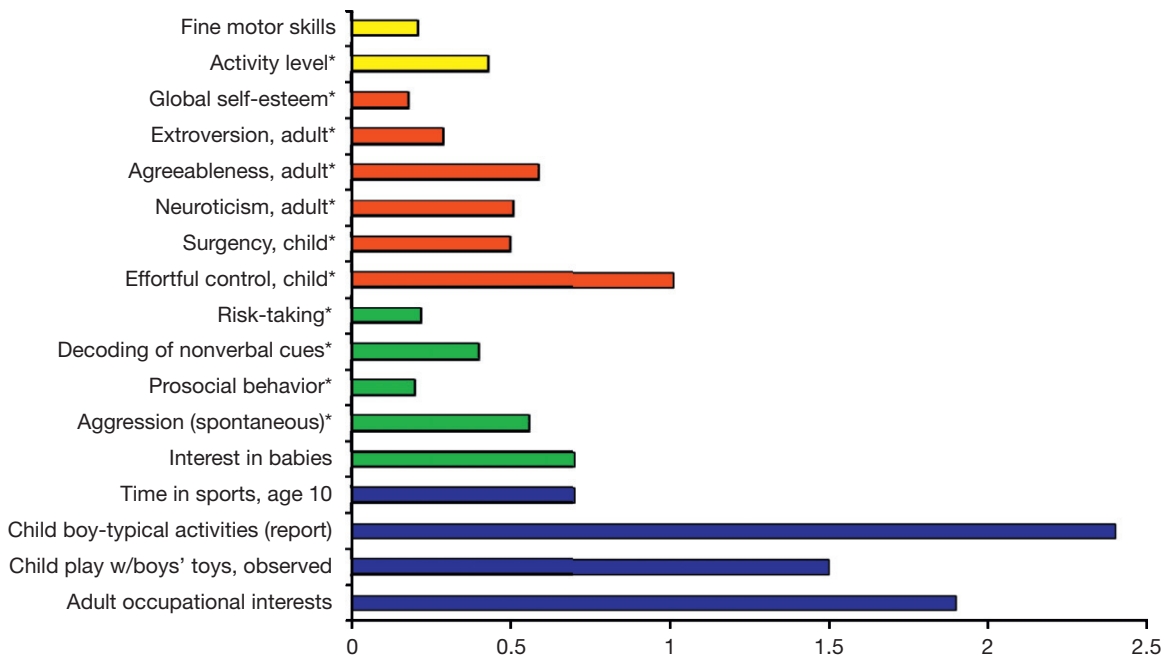
FIGURE 26.3 Sample sex differences in noncognitive characteristics (not including play or sex partners): absolute value of the differences in standard deviation units, *d* (*data from Blakemore et al., 2009*); asterisks (*) indicate results from meta-analyses.

are large to very large. Interests are important because they are reasonably stable, and shape future career choices, especially with respect to domains such as mathematics and the physical sciences (Diekman et al., 2010).

26.2.2.3 Temperament and Personality

Overall, most aspects of temperament show small or no sex differences (Else-Quest et al., 2006). The main exception is effortful control, which shows a moderate advantage for girls, and has been suggested to be consistent with the greater incidence of externalizing disorders in boys, which are characterized by inattentive, antisocial, and aggressive behaviors. In addition, boys have higher levels of surgency than girls, reflecting their greater activity and high-intensity pleasure.

Research on 'the big five' personality factors shows small differences between adult men and women. Costa and colleagues (2001) reported that women were higher than men in neuroticism, agreeableness, and extroversion. They also found cross-cultural similarities in the patterns of sex differences, but the differences between men and women were found to be largest in European and North American countries, and smallest in African and Asian countries.

There are also small sex differences favoring boys and men in global self-esteem, especially after childhood (Kling et al., 1999). Sex differences vary across the different domains of self-esteem, with males having consistently higher appearance-related, personal self, self-satisfaction, and athletic self-esteem, and females having higher ethical and behavioral conduct self-esteem (Gentile et al., 2009).

26.2.2.4 Social Behaviors

The stereotypes about sex differences in social behavior – that girls and women are emotionally expressive and perceptive, and more attuned to babies, and that boys and men take risks and are aggressive – have some basis in evidence, but the differences are not large and depend on context. Consider some examples (for details, see Blakemore et al., 2009). Regarding emotional expression, there is some suggestion that boys and men express more anger and less fear and sadness than girls, but more convincing is evidence that boys come to hide emotions like sadness and fear purposefully, especially in the presence of peers (Kyratzis, 2001). Regarding perceiving emotion in others, girls and women are somewhat more sympathetic, empathic, and accurate at decoding emotions than are boys and men, but the differences are small and depend on how they are measured (larger on self-report than on physiological response) (Eisenberg et al., 2006; McClure, 2000). Girls show more interest in and nurturant interaction with babies than boys do, although the size of the sex difference varies across the particular situations measured in various studies (summarized in Blakemore et al., 2009). Regarding risk-taking, boys are more likely than girls to take risks and to be injured (Byrnes et al., 1999; Morrongiello and Matheis, 2007).

Aggression is one social behavior where sex differences are well known. Aggression is defined as behavior intended to harm others and includes physical, verbal, and indirect aggression. Males are more physically and verbally aggressive than females (Card et al., 2008; Dodge et al., 2006) from childhood through adulthood. Although the social context affects aggression, and the size of the difference varies across age and culture, there are no instances in which females are more directly aggressive than males.

Sometimes physical aggression moves into the domain of seriously antisocial or criminal behavior. Although few people show the type of high levels of physical aggression that would be called violent or antisocial, or at the very extreme, commit murder, the majority of those who do are male, in childhood, adolescence, and adulthood (Archer, 2004; Dodge et al., 2006; Moffitt et al., 2001; Rutter et al., 1998).

Another form of aggression is often called indirect, social, or relational aggression (e.g., Crick, 1995). This form of aggression involves such things as manipulating social relationships or purposefully excluding others. It has been seen as the 'feminine' form of aggression and often (but not always) reported to be more common in girls (see discussion in Blakemore et al., 2009). However, a recent meta-analysis (Card et al., 2008) found no significant differences between boys and girls in indirect aggression from childhood through adolescence.

26.2.2.5 Psychological Disorders

Many forms of serious behavioral problems and mental illness occur at different rates in the two sexes (Hartung and Widiger, 1998). Psychological problems are often described as being internalizing (e.g., anxiety and depression) or externalizing (e.g., conduct disorder, antisocial behavior, including, among other things, criminal acts and excessive aggression, and attention-deficit hyperactivity disorder). The incidence of internalizing problems is higher in girls and women, whereas the incidence of externalizing problems is higher in boys and men (Zahn-Waxler, 1993; Zahn-Waxler et al., 2008); boys are also more likely than girls to have learning and reading disabilities (Blakemore et al., 2009). Disorders that are predominant in males tend to have their onset in childhood (Hartung and Widiger, 1998), whereas the female preponderance of depression and eating disorders begins at puberty (Nolen-Hoeksema and Hilt, 2009).

26.3 EXPLANATIONS FOR PSYCHOLOGICAL SEX DIFFERENCES

Hypothesized causes of psychological sex differences tend to focus on either genetic and biological factors or social and cultural factors. We highlight the key theoretical perspectives focusing on proximal processes; we refer readers elsewhere for discussion and critiques of evolutionary explanations of cognitive and neural sex differences (e.g., Eagly and Wood, 1999; Geary, 1998; Hannagan, 2008; Wood and Eagly, 2002).

26.3.1 Socialization Perspectives

Most work on psychological sex differences comes from a socialization perspective, that is, that sex differences develop as an individual navigates, observes others, is socialized, and internalizes information about the social world. There are several types of socialization theories, differing in the extent to which they emphasize the role of basic social learning mechanisms, subtle socialization practices, social identity (as male or female), cognitive schemas derived from gender identity that guide behavior, and the role of sex-typed social roles and resulting stereotypes and expectancies.

26.3.1.1 Socialization of Noncognitive Sex Differences

Most studies of gender socialization have focused on social behaviors. This literature has been reviewed elsewhere (Blakemore et al., 2009; Martin and Ruble, 2010; Ruble et al., 2006), so we provide a brief summary. In essence, boys and girls are socialized differently in ways that affect a variety of psychological outcomes, with this gendered socialization coming from a variety of sources. Much of the focus has been on socialization by peers and parents, but there are powerful influences from other social forces, including other adults such as teachers, coaches, and clergy, and information received via the many forms of media.

Peers are a key enforcer of sex-typing. Children have strong preferences for interaction with members of their own sex, with these preferences maintained by children themselves and resistant to change by adults (Maccoby, 1998; Ruble et al., 2006). The more children play with others of the same sex, the more they engage in sex-typed activities and play styles (Martin and Fabes, 2001).

Parents also shape sex-typing, as seen in two examples. First, parents influence the career choices of their offspring in several ways: by differential encouragement of sex-appropriate activities, by the attitudes they espouse regarding what is appropriate for boys versus girls, and by the resources they provide to their children (e.g., paying for and providing computer-related materials and encouraging extracurricular involvement in math and science for sons, but not for daughters) (Simpkins et al., 2005). Second, parents socialize emotion differently in their sons and their daughters, through their conversations (e.g., Fivush, 1998; Fivush and Buckner, 2000): With daughters as compared to with sons, parents use more emotion-related words, elaborate their discussion of emotion more extensively, and focus these conversations on the emotional aspects of interpersonal relationships; over time, girls' own discussions include more extensive focus on emotion and emotional issues than do boys' own discussions.

Children also help to socialize themselves through their use of gender schemas. Children are motivated to be like others of their own sex and form cognitive constructions or networks of associations about the sexes that influence their behavior and thinking (Martin et al., 2002). These gender schemas direct children's attention, influence how information is interpreted, organized, and remembered, and guide behavior with objects and people; specifically, children selectively attend to and remember sex-typed information and show biases towards members of their own group (for review, see Martin et al., 2002). Many studies confirm the power of gender schemas to influence many aspects of behavior and thinking, including children's toy play, play partners, the ability to learn about activities that are traditionally sex-typed for the other sex, and impressions of others (reviewed in Blakemore et al., 2009; Martin et al., 2002; Ruble et al., 2006).

26.3.1.2 Socialization of Cognitive Sex Differences

Socialization perspectives have been applied less to cognitive abilities than to other sex-typed characteristics. Nevertheless, there are several types of evidence confirming the importance of social influences on sex-typed abilities.

Sex-typed academic skills, such as math and language, are influenced by family socialization. For example, although parents think that academic achievement is equally important for sons and daughters, they provide support for extracurricular involvement in math and science more for sons than for daughters (Simpkins et al., 2005), and parents' subtle beliefs about the inherent superiority of boys in such domains appears to undermine girls' subsequent academic performance, especially in math (Eccles et al., 2000).

Sex differences in spatial ability have been seen to depend on socioeconomic status (SES), with differences apparent in children from middle and high SES backgrounds, but not in children from low SES backgrounds (Levine et al., 2005). Such SES effects were suggested to result in part from access to experiences that facilitate spatial ability.

Spatial abilities have been suggested to develop from childhood sex-typed activities (e.g., Connor and Serbin, 1977, reviewed in Lawton, 2010). In particular, boy-typed toys and activities (such as building with Lego) are seen to encourage manipulation and exploration of the environment, and some have claimed that sex differences in spatial abilities would be reduced or even eliminated if girls were encouraged to play more with boys' toys (Halpern, 1986; Tracy, 1990). Evidence does show a weak-to-moderate link between spatial ability and aspects of sex-typed activities (e.g., Newcombe et al., 1983), but there is some variability and inconsistency that likely reflects methodological and conceptual issues (Baenninger and Newcombe, 1989; Voyer et al., 2000). It is important to note that these associations are not evidence of causation: engagement in boy-typed activities might enhance spatial ability or instead reflect that ability, that is, children with high spatial ability might be attracted to toys that allow manipulation and exploration. Some longitudinal data suggest that the causal path is from abilities to activities rather than the reverse (Newcombe and Dubas, 1992).

It is therefore important to note direct experimental evidence that spatial ability can be enhanced by experience. In particular, spatial ability can be improved through practice and training, with generalization beyond training stimuli. For example, playing an action video game was seen to improve both spatial attention and mental rotation ability (Feng et al., 2007). Training benefits both sexes, with women sometimes benefiting more than men, so that training may eliminate a sex difference in this domain (Lawton, 2010; Uttal et al., 2012).

Finally, stereotypes that emphasize women's cognitive inferiority appear to impair their performance (Steele, 1997). This has been demonstrated in studies that involve experimental manipulations, as illustrated for both math and spatial ability. Women who were told that sex differences in math have genetic causes performed worse on math tests than those who were told that the differences have experiential causes (Dar-Nimrod and Heine, 2006). Women who were told that men outperform women on spatial tasks performed worse on a mental rotations test than women who received neutral information, and the poorer performance of the group given negative stereotypes appeared to reflect increased emotional load (Wraga et al., 2007).

26.3.2 Genetic Perspectives

It is reasonable to expect that sex-related characteristics would be influenced by genes on the sex chromosomes, reflecting sex differences in sex chromosome composition (XX for typical females, XY for typical males). Work in individuals with sex chromosome abnormalities using sophisticated approaches has provided intriguing evidence that genes on the X chromosome

may influence aspects of cognition, including aspects of spatial ability (Ross et al., 2006). Evidence in rodents suggests that genes on the Y chromosome influence sex-typed behavior, including spatial ability and parenting (Arnold, 2009; Arnold and Chen, 2009). There are very limited human data on this topic, but they do not currently show direct effects of genes on the Y chromosome: Women with complete androgen insensitivity syndrome, who have a Y chromosome but no effective androgen exposure, reported similar childhood and adulthood gender role behavior to unaffected women (Hines et al., 2003a).

26.3.3 Hormonal Perspectives

26.3.3.1 Principles

Most of the research on biological mechanisms underlying gendered characteristics has focused on sex hormones, primarily androgens (including testosterone) and estrogens. This research is rooted in the work of Phoenix, Goy, and colleagues (Gibber and Goy, 1985; Phoenix et al., 1959, 1973), showing the long-lasting effects of early sex hormones on sex differences in behavior in rodents and primates, and in the subsequent work of Money and Ehrhardt (1972) in human beings. Hormones affect behavior in two ways (Becker et al., 2008; Goy and McEwen, 1980). First, sex hormones produce permanent changes to brain structures and the behaviors they subserve ('organizational' effects). Such effects usually occur early in life (during the prenatal period in human beings), although adolescence may also be an important organizational period (Schulz et al., 2009; Sisk and Zehr, 2005). Second, sex hormones produce temporary alterations to the brain and behavior (through ongoing changes to neural circuitry) as the hormones circulate in the body throughout adolescence and adulthood ('activational' effects). The main distinctions between organizational and activational effects concern timing and permanence, although these distinctions are not absolute (Arnold and Breedlove, 1985).

26.3.3.2 Evidence for Hormonal Influences on Nonhuman Sex-typed Behavior

Studies in many nonhuman animal species show that sex hormones are crucial for behavioral sex differences. Much work has confirmed and extended the early work of Phoenix, Goy, and colleagues, showing that hormones present during early life organize the brain so that they have long-lasting effects (Becker et al., 2002, 2008; Ryan and Vandenbergh, 2002; Wallen, 2005, 2009). These studies generally involve experimental manipulations of hormones (e.g., injecting females with testosterone, castrating males), but behavior has also been seen to be influenced by naturally occurring variations in hormones,

such as those that result from an animal's position in the uterus, particularly the sex of its littermates (for reviews, see Clark and Galef, 1998; Ryan and Vandenbergh, 2002).

Even in nonhuman animals, however, the effects are complex. For example, studies in monkeys highlight two aspects of this complexity: (a) there are several sensitive periods for androgen effects on behavior, even during the prenatal period, with some behaviors masculinized by exposure early (but not late) in gestation, and other behaviors masculinized by exposure late (but not early) in gestation (Goy et al., 1988); and (b) environmental context modifies behavioral effects of hormones (Wallen, 1996).

Further, sex hormones may continue to exert organizational effects well beyond early life. Evidence from rodents indicates that puberty is another organizational period, with sex hormones at puberty producing permanent changes to the brain and behavior (Schulz et al., 2009; Sisk and Zehr, 2005).

There is also an extensive literature showing that sex hormones are necessary for the expression of sex-typed behaviors in adulthood (activational effects). Much work has focused on the importance for sexual behavior of testosterone in males and estradiol in females, but these hormones also play a role in the expression of nonsexual behaviors in adult animals, such as maternal behavior and aggression (Becker et al., 2002, 2008).

26.3.3.3 Methods for Studying Early Hormonal Influences on Human Behavior

Studies in people cannot involve experimental manipulations of hormones, but have taken considerable advantage of natural experiments, individuals whose hormone levels were atypical for their sex during early development as a result of a genetic disease or maternal ingestion of drugs during pregnancy to prevent miscarriage (for details, see Blakemore et al., 2009). The most extensively studied natural experiment is congenital adrenal hyperplasia (CAH), a genetic disease resulting in exposure to high levels of androgens beginning early in gestation because of an enzyme defect affecting cortisol production. If human psychological sex differences are affected by androgens present during critical periods of development (as occurs in nonhuman animals), then females with CAH should be behaviorally more male-typed and less female-typed than a comparison group of females without CAH.

Because CAH is not a perfect experiment (e.g., high levels of prenatal androgen also lead to masculinized genitalia, which might affect socialization, and CAH requires lifelong treatment with cortisone), it is important to seek converging evidence from other sources. Such evidence has been obtained for a number of behavioral domains from other natural experiments and from normal individuals with typical variations in hormones. The latter includes those whose hormones have been directly measured (in amniotic fluid) and those whose hormones have been inferred (by virtue of sharing a uterine environment with an opposite-sex twin).

We briefly summarize the evidence that prenatal hormones – particularly androgens – influence human psychological sex differences and highlight key findings and issues. This evidence has been discussed in detail elsewhere (Berenbaum, 2006; Berenbaum and Beltz, 2011; Blakemore et al., 2009; Cohen-Bendahan et al., 2005; Hines, 2010).

26.3.3.4 Prenatal Hormone Influences on Human Behavior: Noncognitive Sex Differences

Data from several groups and countries with a variety of sound methods (including observations, tests, self-reports, and parent-reports) make clear that girls and women with CAH are more male-typed and less female-typed in aspects of their feelings, preferences, and behavior than are girls and women without CAH (in most studies, their unaffected sisters; reviewed in Berenbaum and Beltz, 2011; Blakemore et al., 2009; Hines, 2010). The largest difference between females with and without CAH is in sex-typed activity interests and engagement: girls and women with CAH prefer and are more likely to participate in male-typed activities from childhood through adulthood. They also have male-typed occupational interests; for example, females with CAH reported more interest in occupations that involve working with things (versus people) than unaffected female siblings (Beltz et al., 2011). The male-typed activity preferences and engagement in girls with CAH are directly associated with prenatal androgen and have not been shown to be influenced by parents' behavior (Meyer-Bahlburg et al., 2006; Nordenström et al., 2002; Pasterski et al., 2005). Females with CAH are sex-atypical in other domains (reviewed in Berenbaum and Beltz, 2011; Blakemore et al., 2009; Hines, 2010). Compared to typical females, females with CAH are more aggressive and less interested in babies and are more likely to have bisexual or homosexual orientation (although most are exclusively heterosexual). These masculinized characteristics stand in contrast to female-typical identity in the overwhelming majority of females with CAH (Dessens et al., 2005).

Data from other natural experiments also show that male-typical prenatal androgen levels are associated with male-typed activity interests and nonheterosexual orientation (e.g., Meyer-Bahlburg, 2005, reviewed in Berenbaum and Beltz, 2011; Blakemore et al., 2009). But the most compelling converging evidence comes from a study linking amniotic testosterone levels to activity interests in boys and girls at ages 6–10 (Auyeung et al., 2009): the most male-typed interests

and characteristics (as reported by parents on a widely used measure) were found in children who had had high levels (for their sex) of naturally occurring prenatal testosterone. Unfortunately, there is little other good evidence about links between amniotic testosterone and other sex-typed characteristics in typical samples; the few existing studies had small samples and other methodological limitations.

There has also been interest in effects of early hormones on sex differences in psychopathology. Early organizational androgens have been hypothesized to contribute to the male vulnerability for childhood disorders (e.g., Baron-Cohen et al., 2004; Martel et al., 2009); however, there has been little consideration of the ways that different disorders would be affected by hormones. For example, autism has been claimed to reflect 'the extreme male brain' and therefore result from exposure to high prenatal androgens (Baron-Cohen et al., 2004), but many other disorders show similar male predominance and have been suggested by others to also result from high prenatal androgens (e.g., Martel et al., 2009).

26.3.3.5 Prenatal Hormone Influences on Human Behavior: Cognitive Sex Differences

Evidence from multiple sources provides moderate support for the notion that prenatal androgens influence later spatial and related abilities. Nothing is known about prenatal hormonal effects on mathematical abilities or on abilities that show a female advantage, because the sex differences are small to moderate, and it has been hard to accrue large enough samples.

Females with CAH have been found to have higher spatial ability than their sisters in childhood, adolescence, and adulthood (Berenbaum et al., 2012; Hampson et al., 1998; Hines et al., 2003b; Mueller et al., 2008; Resnick et al., 1986), with a meta-analysis suggesting that the effect is small to moderate (Puts et al., 2008). The relatively small size of the effect may explain why the effect is not always seen (e.g., Hines et al., 2003b; Malouf et al., 2006).

Confirming evidence for the effects of androgen on spatial ability comes from individuals at the other end of androgen levels: males with low early androgen levels due to idiopathic hypogonadotropic hypogonadism (IHH) have lower spatial ability than controls (Hier and Crowley, 1982). Importantly, the external genitals of males with IHH appear typical, suggesting that enhanced spatial ability in females with CAH is not due to social responses to their genitals.

There are now several studies of androgen effects on spatial ability in typical samples that provide converging evidence for prenatal androgen effects on spatial ability. In three studies of opposite-sex twins, females with a male co-twin (who are thought to have above-average prenatal exposure to testosterone) have been shown to have higher spatial ability than females with a female co-twin (Cole-Harding et al., 1988; Heil et al., 2011; Vuoksimaa et al., 2010). But, prenatal hormone influences are confounded with postnatal socialization in some of these findings because females with a male co-twin are reared with a male sibling of the same age. Evidence against socialization effects comes from women with slightly older siblings: those with a brother did not have better spatial ability than those with a sister (Heil et al., 2011). In one study of amniotic hormones, testosterone was associated with some indices of spatial ability in girls at age 7: compared to girls who had low amniotic testosterone, girls with high levels showed faster, but not more accurate, mental rotation; the effect was seen only in girls who showed evidence of using a mental rotation strategy (Grimshaw et al., 1995b).

26.3.3.6 Adolescent Hormone Influences on Human Behavior

In light of the recent animal evidence on the behavioral importance of organizational hormones at puberty, there has been increased attention to the effects of pubertal hormones on the human brain and behavior (see also Section 26.5). With respect to behavior, there is considerable speculation – but not a lot of data – about the ways in which changes at adolescence are triggered by the surge in sex hormones at that time, including girls' increased vulnerability to depression and eating disorders (Crick and Zahn-Waxler, 2003; Martel et al., 2009) and boys' increased risk taking and substance use (Forbes and Dahl, 2010; Steinberg, 2008). This is an area of active investigation, thus it is likely we will know much more about pubertal hormone effects on the brain and behavior within the next decade.

26.3.3.7 Circulating Hormone Influences on Human Behavior

There is an extensive literature (primarily in adolescents and adults) linking circulating levels of sex hormones (especially estradiol and testosterone) to sex-typed characteristics, primarily aggression, mood, and cognitive abilities (reviewed in Buchanan et al., 1992; Hampson, 2007; Maki and Sundermann, 2009; Puts et al., 2010). This work focuses on activational (transient) effects of hormones, so that behavior changes when hormone levels change. Findings are complex and difficult to summarize briefly (see reviews above for details). Much of the complexity reflects small effects, reliance on observational studies in adults, and bidirectional effects of behavior and hormones (e.g., aggressive behavior can increase testosterone). Hormones do not produce simple changes in behavior, and the most valuable studies are those that examine the ways in which hormones act indirectly and interact with social factors to change sex-related characteristics.

There is some consistency in the findings regarding cognitive effects of circulating sex hormones, with data coming from studies of natural variations in hormones across individuals and within individuals (e.g., in association with the menstrual cycle) and effects of hormone replacement (in association with aging or surgical removal of the ovaries). Findings are complex (for reviews, see Hampson, 2007; Maki and Sundermann, 2009), but generally suggest that spatial ability is facilitated by testosterone in the moderate range (levels that are high for females and low for males) and verbal memory is facilitated by estradiol, especially in postmenopausal women who are relatively young or recently menopausal. Nevertheless, links between cognition and hormones are not always found, probably due to factors that modify the effects of both hormones (e.g., diet) and cognition (e.g., experiences).

26.3.4 Integrated Perspectives

It is clear that sex-typed characteristics are influenced by multiple factors, and it is unfortunate that most studies focus on a single set of factors, rather than examining them in concert. As we have argued elsewhere (Berenbaum et al., 2011), sex differences can best be understood by integrating the different perspectives; focusing on only one set of causes (either social or biological) can lead to a distorted or even misleading understanding of sex-typed processes.

Consider spatial ability as an example of the ways in which an understanding of sex differences could be enhanced by attention to both biology *and* social experiences (for detailed discussion and other examples, see Berenbaum et al., 2011). As discussed above, evidence makes it clear that spatial ability depends on social experiences, genes on the X chromosome, and sex hormones during prenatal development and again in adult life. But spatial ability almost certainly develops from *joint* influences of biology and social experiences, as illustrated in two ways. First, biological influences on spatial ability are likely mediated through experience. As noted above, girls who are exposed to high levels of androgen during prenatal life (because of normal variation or CAH) are more likely than girls with low levels to play with boys' toys, and those toys may facilitate the development of spatial ability (e.g., Newcombe et al., 1983). Preliminary evidence from females with CAH does indeed indicate that their enhanced spatial abilities are in part mediated by their masculinized activity interests (Berenbaum et al., 2012). Second, biological predispositions likely facilitate learning. Although existing training studies are not compelling in this regard (men, who have high androgen levels, do not appear to be more likely to benefit from practice than women, who have low androgen

levels), the situation might differ in childhood, when abilities are developing, and on tests that do not show ceiling effects. This question can be studied in girls with CAH and in typical children, by examining the effects of practice at varying ages and with varying environmental experiences (e.g., as a function of SES).

26.4 BRAIN SEX DIFFERENCES: NATURE, DEVELOPMENT, AND CONSEQUENCES

The brains of men and women, and of boys and girls, are similar in many ways, but there are some systematic differences in anatomical structure, physiological functioning, and development. An understanding of these differences – and what causes them – should provide insight into the mechanisms underlying sex differences in human health, disease, and behavior, including the characteristics discussed above (Cosgrove et al., 2007; McCarthy and Arnold, 2011).

In this section, we review the work on human brain sex differences. We focus on topics where there is converging evidence for brain sex differences, but we also present some exciting new findings that will likely spark future research. Most of the work reviewed comes from studies using magnetic resonance imaging (MRI), as it is the dominant research tool in human developmental neuroscience (Casey et al., 2005; Luna et al., 2010), but we also consider work using other techniques, such as positron emission tomography (PET), perceptual asymmetries, and post mortem examinations.

26.4.1 Issues in Studying Brain Sex Differences

MRI is widely used as a measure of brain anatomy and physiology. Structural MRI (sMRI) provides measures of brain morphology and architecture (e.g., volumes of gray matter, white matter, and subcortical structures). Blood oxygen level-dependent (BOLD) functional MRI (fMRI) is a measure of change in blood oxygenation thought to reflect neural activity. Diffusion tensor imaging (DTI) is the most frequently used assessment of water diffusion in the brain, thought to reflect white matter microstructure and thus information transmission among brain regions. All MRI measures – sMRI, fMRI, and DTI – are indirect measures of brain structure and function, involving multiple assumptions and inferences, and each reflects multiple dynamic processes occurring at cellular and subcelluar levels (for discussion relevant to developmental science, see Casey et al., 2005; Paus, 2010).

The analysis of MRI data, particularly functional data, is complex and based on multiple assumptions, partly

because assessments are indirect. The brain is typically partitioned into volumetric pixels, or voxels, and statistics are conducted on each voxel as if it were independent of all others. This 'mass univariate approach' can result in a score of false positives unless appropriate corrections to p-values are made for multiple comparisons (Friston, 2004). In studies linking behavior to brain activation, findings may be spurious if only voxels exceeding some preset threshold are examined (Vul et al., 2009). This is essentially a selection bias: only data from voxels reflecting significant brain activation are examined in relation to behavior. This problem can be avoided through *a priori* selection of brain regions of interest (ROIs) for analyses (Poldrack, 2000; Vul et al., 2009).

Concerns have been expressed about the interpretations of findings of brain sex differences (Fine, 2010; Jordan-Young, 2010). Such problems appear to result from the inappropriate use of data, rather than from the data themselves. First, people may over-interpret brain images because they are compelling; research containing irrelevant neuroscience explanations and brain images is rated by nonexperts as more satisfying or reasonable than accurate work without such information (Beck, 2010; McCabe and Castel, 2008; Weisberg et al., 2008). Second, brain sex differences are often interpreted in simplistic ways. For example, a bigger brain is not necessarily a better brain (see Section 26.4.2.1), and brain sex differences are not indicators of predetermined behavioral inequalities (see also McCarthy and Arnold, 2011; Poldrack, 2000). Third, brain sex differences need to be considered in conjunction with behavioral sex differences (see Sections 26.4.2.5 and 26.4.3).

As we discuss below, there is much careful and important work demonstrating brain sex differences. Research questions developed from a clear conceptual framework are often investigated using sound methodology and a careful approach to examining brain–behavior relations. Inferences are often balanced and appropriate, and there is considerable convergence of evidence. Of course, as in any area of science, not all studies are perfect, but limitations in methodology and inference are no more prevalent or problematic in this field than elsewhere (Fiedler, 2011).

26.4.2 Sex Differences in Brain Structure and Their Development

An understanding of brain sex differences requires consideration of development. Some of the most compelling work on brain–behavior relations has shown both a change in structural sex differences across development and the importance of considering developmental trajectories (pattern of brain changes over time), not just a single measurement (see Rubenstein and Rakic, 2013). For example, general intelligence has been shown to relate to changes in cortical thickness across childhood and adolescence, but not to absolute measures of cortical thickness at a given age (Shaw et al., 2006); compared to typical children, children with attention-deficit hyperactivity disorder have delayed trajectories of cortical thickness maturation (Shaw et al., 2010). Thus, sex differences in brain development are best examined in longitudinal neuroimaging studies; however, there are many more studies of sex differences at a single point in time, so we review those studies (typically done in adults) as well as the longitudinal neuroimaging data. We first review findings of sex differences in brain structure and then examine how structural differences relate to behavioral sex differences.

26.4.2.1 Brain Volume

There are sex differences in intracranial and cerebral volume, with both approximately 10% larger in males than in females. These differences are seen in measurements made on postmortem brains (Holloway, 1980) and in live ones (using MRI) (De Bellis et al., 2001; Giedd and Rapoport, 2010; Giedd et al., 1997; Goldstein et al., 2001; Lenroot and Giedd, 2010; Lenroot et al., 2007; Nopoulos et al., 2000; Sowell et al., 2002); they are also seen in several nonhuman primate species (Falk et al., 1999; Holloway, 1980). The human differences appear to be primarily due to the larger occipital and frontal poles of men compared to women (Sowell et al., 2007). The differences in brain size are due in part to sex differences in body size, reflecting overall growth differences (Halpern, 2012; Holloway, 1980; Peters, 1991; Peters et al., 1998).

The brain reaches about 95% of its adult size by age 6, but the relative proportions of gray matter and white matter continue to change throughout childhood and adolescence. The peak cerebral volume occurs about 4 years earlier in girls than in boys, but boys have a larger absolute cerebrum size than girls throughout development (Giedd and Rapoport, 2010; Lenroot et al., 2007).

The implications of brain size sex differences for brain function or behavior, however, are not clear (see also Section 26.4.2.5). Sex differences in the size of other body structures (e.g., men's larger hearts and noses) do not translate into sex differences in function. Further, a larger brain does not necessarily mean a smarter brain. Although there is a moderate association between brain size and intelligence (Flashman et al., 1997; Luders et al., 2009b), there are no sex differences in general intelligence, and neural connectivity (rather than size) is key to understanding the brain substrates of intelligence (Song et al., 2008; van den Heuvel et al., 2009). Interpretations of structural size differences are complicated for several reasons: normal brain maturation involves cell death and synaptic pruning, reducing brain size; brain

size may be larger in individuals with developmental disorders, such as autism (Shaw et al., 2010; Sowell et al., 2001, 2002); there are dynamic relations between experiences and brain anatomy (e.g., taxi driving experience is associated with hippocampal shape) (Maguire et al., 2000, 2003).

The sex difference in body size creates difficulties in studying sex differences in brain size, which, in turn, creates difficulties in studying other aspects of brain sex differences, leading to controversies over whether to correct for body size and overall brain size. Some have argued that sex differences in brain size are best corrected by body weight or height (Halpern, 2012; Holloway, 1980). Others have claimed that the relation between body height or weight and brain size is weak (Peters, 1991), particularly because there is great variation in human body size and type (Peters et al., 1998). Further, the relation between brain and body size changes across development (Giedd and Rapoport, 2010; Lenroot and Giedd, 2010), suggesting that brain–body size corrections should only be made in adult samples.

There are several ways to correct for sex differences in intracranial or cerebral volume in order to examine sex differences in specific brain structures (see Bishop and Wahlsten, 1997). First, brain volume can be covaried. This approach is most appropriate if there is a linear relationship between brain size and the size of the brain structure or region being investigated, and it can misrepresent sex differences if the relation is present in only one sex. Second, a ratio can be computed, reflecting the volume of the structure or regions being investigated as a proportion of brain size; this approach is easy to understand, but its anatomical interpretation is unclear. Finally, recent innovative approaches have been suggested, including the use of different numerical scaling factors for different characteristics of brain anatomy because larger brains are not uniform expansions of smaller brains; for example, there is greater relative increase in cortical surface area than cortical thickness with brain size increases (Im et al., 2008). Longitudinal studies overcome the problem by allowing examination of within-individual change across time and subsequent comparison of rates of change between the sexes (e.g., Thambisetty et al., 2010).

26.4.2.2 Regional Structure Volume

There are several consistently replicated sex differences in the size of human regional brain structures. But these effects are not always detected, likely because they are small and approaches to correcting for sex differences in brain size vary across studies. Generally, as detailed below, some key regions of the brain implicated in interhemispheric communication and memory (e.g.,

hippocampus and caudate nuclei) are larger in women than men, and other subcortical regions implicated in affective and sexual behaviors (e.g., amygdala and hypothalamus) are larger in men than women.

26.4.2.2.1 SEX DIFFERENCES IN INTERHEMISPHERIC COMMISSURES

Several studies have investigated sex differences in interhemispheric commissures (fiber bundles spanning the two halves of the brain). Commissures are important for facilitating information flow across hemispheres and thus for promoting cognitive function (Bryden, 1982; Kimura, 1999).

There has been particular focus on sex differences in the most posterior portion of the corpus callosum (CC), the splenium, following an early histological report of a sex difference in this region (De Lacoste-Utamsing and Holloway, 1982). A meta-analysis of 49 studies concluded that there are no systematic sex differences in this structure when appropriate corrections are made for the sex difference in brain size (Bishop and Wahlsten, 1997), and recent MRI studies support this finding (Leonard et al., 2008; Luders et al., 2006b). Nonetheless, research with large, adult samples using a sophisticated analysis technique (in which derivations of an individual's CC from a template CC are captured at many points), indicates that women do, in fact, have larger splenia than men (Davatzikos and Resnick, 1998; Dubb et al., 2003). Other research has positively linked the size of the splenium in women (but not men) to cognitive abilities, such as verbal fluency, two-dimensional mental rotations, and memory (Davatzikos and Resnick, 1998; Hines et al., 1992); however, these links are not consistently seen in children and adolescents (e.g., Luders et al., 2011).

The CC develops in a rostral-to-caudal direction throughout childhood and early adolescence, and the rate of growth may be greater in girls than in boys (Luders et al., 2010; Thompson et al., 2000). This sex difference is particularly striking because boys have faster overall rates of white matter development than girls (Section 26.4.2.4). Even from late adolescence through late adulthood, the splenium appears to increase in size in women more than in men (Dubb et al., 2003).

There are sex differences in the anterior commissure (connecting the right and left temporal lobes) and massa intermedia (connecting the right and left thalamus), but less is known about their functional significance than that of the CC. Both structures are generally found to be larger in women than men (Allen and Gorski, 1991, 1992; Kimura, 1999). The massa intermedia is also more frequently absent in men than in women (Rabl, 1958), and absence of this structure is linked to greater performance IQ scores for men, but not for women (Lansdell and Davie, 1972).

26.4.2.2.2 SEX DIFFERENCES IN STRUCTURES INVOLVED IN LEARNING AND MEMORY

Several brain structures implicated in learning and memory are also larger in females than males, consistent with the female advantage in memory (Section 26.2.1.4). The hippocampus, which is important for memory formation, retention, and recall, is larger in women than men (Cahill, 2005; Filipek et al., 1994; Goldstein et al., 2001; Halpern, 2012; Lenroot and Giedd, 2010), though this difference is most consistently reported in children and adolescents, perhaps because the hippocampus is generally found to grow at a faster rate and thus to mature earlier in girls than boys (Giedd et al., 1997; Lenroot and Giedd, 2010). The caudate nuclei, which are part of the basal ganglia and implicated in learning and memory, are also larger in females than males; this finding has been reported in both children (Giedd et al., 1997; Sowell et al., 2002) and adults (Filipek et al., 1994; Goldstein et al., 2001). Caution must be used when interpreting the implications of these findings because the sex difference in verbal memory remained in a sample of men and women who had left anterior temporal lobectomy, suggesting that other brain regions and sex differences in strategy are also important for sex differences in memory (Berenbaum et al., 1997).

26.4.2.2.3 SEX DIFFERENCES IN SUBCORTICAL STRUCTURES INVOLVED IN AFFECTIVE AND SEXUAL BEHAVIORS

Brain structures consistently found to be larger in men than women include regions of the hypothalamus and the amygdala. Sex differences in the human hypothalamus parallel early studies showing a very large sex difference in the rodent preoptic hypothalamus (Gorski et al., 1978). In particular, one of the four interstitial nuclei of the anterior hypothalamus (INAH-3) is larger in men than women (reviewed in Halpern, 2012; Kimura, 1999; LeVay, 1991). There are also reports that some regions of the bed nucleus of the stria terminalis (BNST), the central portion of the connection between the hypothalamus and amygdala, are larger in men than women (Allen and Gorski, 1990; Zhou et al., 1995). Although the functional implications of these sex differences are unclear, there is some suggestion that the INAH and BNST play a role in gender identity and sexual orientation (for discussion, see Hines, 2011; Savic et al., 2010).

The amygdalae, a pair of bilateral structures in the medial temporal lobe, are also larger in boys and men than in girls and women (Cahill, 2005; Goldstein et al., 2001; Halpern, 2012; Lenroot and Giedd, 2010) and develop faster in boys than in girls (Giedd et al., 1997; Lenroot and Giedd, 2010). They are thought to be important for the detection of and behavioral response to affective visual cues, perhaps because of their connectivity to many cortical and subcortical regions (Pessoa and Adolphs, 2010).

26.4.2.3 Gray Matter

There are sex differences in gray matter, with girls and women having relatively more gray matter than boys and men across the lifespan, particularly in parts of the frontal, temporal, and parietal lobes (Gur et al., 1999; Lenroot et al., 2007; Leonard et al., 2008; Luders and Toga, 2010; Luders et al., 2002; Paus, 2010). Relatedly, women have greater cortical thickness than do men in some areas of the brain, particularly in the frontal and parietal lobes. Supporting evidence comes from several different samples and research methodologies, including MRI combined with surface morphometry (Im et al., 2006; Lv et al., 2010), pattern algorithms (Luders et al., 2006a; Sowell et al., 2007), and tissue segmentation (Koscik et al., 2009). Some histological findings are inconsistent, but their interpretation is complicated by small sample sizes (e.g., Rabinowicz et al., 1999).

There are parallel differences in cortical complexity, or patterning of cerebral convolutions, with women showing greater complexity than men, particularly in the frontal and parietal lobes (Luders et al., 2004, 2006c). Findings of sex differences appear to vary with method: differences favoring females have been found using a new mesh-based approach (in which the convolutions at several thousand surface points are estimated from three-dimensional brain scans), but not when using the gyrification index (ratio of cortical surface to visible gyral surface, calculated from two-dimensional postmortem brain slices) (Zilles et al., 1988).

Gray matter develops in an inverted U-shaped trajectory across childhood and adolescence, increasing until puberty and then decreasing through early adulthood (Giedd and Rapoport, 2010; Giedd et al., 1999; Lenroot and Giedd, 2010; Lenroot et al., 2007). The shape and timing of the peak in gray matter trajectories differ across brain regions: parietal lobe volumes peak first, followed by frontal and temporal lobe volumes. Relatedly, cortical maturity, marked by decreases in cortical density, occurs in a specified pattern: the medial sensorimotor cortex matures first, with development proceeding in rostral and lateral directions, such that the prefrontal and lateral temporal cortices are the last regions to mature (Gogtay et al., 2004). This reduction in gray matter density, which occurs after pubertal onset, likely reflects the elimination of irrelevant brain connections and strengthening of relevant ones (i.e., pruning). The sexes have similarly shaped trajectories of gray matter development across all brain regions, but girls have an earlier average peak than boys, consistent with their earlier pubertal maturation. Generally, girls show a peak in regional gray matter between 8 and 10 years of age, whereas boys show a peak between 9 and 11 years of age (Lenroot et al., 2007).

26.4.2.4 White Matter

There is not clear consistency from MRI studies regarding sex differences in overall brain proportions of white matter. Some evidence indicates that men have a greater proportion of white matter than do women (Allen et al., 2003; Gur et al., 1999), but the difference is not always found and inconsistencies are not explained by differential corrections for the sex difference in brain size (Luders et al., 2002; Nopoulos et al., 2000). Women are rarely found to have greater white matter volume than men, suggesting that small samples make it difficult to consistently detect the increased white matter in men compared to women. Inconsistencies may also reflect age differences; sex differences in the proportion of brain white matter generally emerge in adolescence and persist through adulthood (Paus, 2010).

Converging evidence from MRI also suggests no sex differences in fractional anisotropy (FA), which is thought to reflect directed information transmission along white matter paths. This evidence comes from large, cross-sectional DTI studies (Eluvathingal et al., 2007; Giorgio et al., 2008; Lebel et al., 2008).

White matter volume increases linearly through childhood and into adulthood, and this pattern is consistent across brain regions (Giedd et al., 1999; Lenroot et al., 2007). Girls and boys both experience linear increases in white matter volume, but boys have a more rapid rate of increase compared to girls, particularly in adolescence (Lenroot et al., 2007). FA similarly increases across early childhood and into adulthood in an inferior-to-superior and posterior-to-anterior fashion (Colby et al., 2011); white matter connections around subcortical structures and in the CC undergo the greatest change across development, and frontal–temporal tracts are the last to mature (Eluvathingal et al., 2007; Giorgio et al., 2008; Lebel et al., 2008). Increases in FA may mark a transition from functional localization to distributed neural network functioning in the developing brain. For example, adolescents show a decrease in frontal gray matter density as FA increases in pathways connecting frontal regions to other brain areas (Giorgio et al., 2008). The ways in which sex interacts with age changes in FA are still unclear (for a review, see Schmithorst and Yuan, 2010): there are few patterns among the observed sex differences, and inconsistent findings likely reflect samples of varying age, the sex difference in white matter development, differences in FA measurement across studies (e.g., analyses at the level of voxels versus ROIs), and problems inherent in FA methodology (e.g., measurement of perpendicular fiber tracts within a voxel).

26.4.2.5 Implications of Sex Differences in Brain Structure

Some – but not all (e.g., Luders et al., 2009a) – of the sex differences in brain morphology might result from the different shaping of larger versus smaller brains (Allen et al., 2003; Im et al., 2008; Luders et al., 2002, 2010; Seldon, 2005; Zhang and Sejnowski, 2000). In larger as compared to smaller brains, the cortex tends to be flatter and thinner because it fills a larger intracranial space; this is consistent with reports of greater cortical thickness and complexity in women than men. There is also more white matter in larger brains because longer axonal connections are made to cortical regions that are farther apart than in smaller brains. This is consistent with evidence that men have greater white matter volumes than women.

What do sex differences in brain structure mean for cognitive sex differences? Compared to women, men appear to have larger regions of the parietal lobe, which is the primary brain area implicated in spatial ability (Brun et al., 2009). Parietal lobe surface area is, in fact, positively related to mental rotations performance in men, whereas parietal lobe gray matter volume is negatively related to mental rotations performance in women (Koscik et al., 2009); this suggests that different parietal lobe morphology subserves mental rotations performance in men and women, but it does not indicate whether men and women equally engage parietal regions during mental rotations tasks (this requires data on brain activation). There is also evidence from structural studies that some brain regions implicated in language, especially the temporal lobe, are larger in women than men (Brun et al., 2009; Harasty et al., 1997). But, these studies are difficult to interpret because verbal ability was not assessed. Sex differences in brain activation during spatial and language tasks are reviewed below (Sections 26.4.3.1 and 26.4.3.2, respectively).

It is probable that not all structural sex differences have behavioral significance, as there are likely multiple paths to the same outcome (De Vries, 2004; McCarthy and Arnold, 2011); this also appears to be the case for other bodily organs (e.g., the heart). Despite large variations in structure, brain function is remarkably similar and stable across people (Sporns, 2011). If this 'functional homeostasis' is maintained, then links between brain structure and behavior will not always exist.

26.4.3 Sex Differences in Brain Function (Activation)

There is a considerable literature examining sex differences in brain function as measured by task-specific activation (fMRI). The most meaningful work relates brain activation to task performance. An important issue concerns the sex difference on the behavioral outcome of interest. If men and women perform at different levels, brain activation differences might tell us about the neural substrates of the performance difference. If men and women perform at similar levels, brain activation

patterns might tell us about the (potentially different) processes or strategies they use to arrive at the same outcome.

26.4.3.1 Spatial Abilities

There has been interest in finding the neural correlates of the male advantage in spatial ability described in Section 26.2.1.1. Generally, in both sexes, spatial processing is associated with activation of the parietal lobes as well as temporal, premotor, and extrastriate areas (Butler et al., 2006; Christova et al., 2008; Halari et al., 2006; Hugdahl et al., 2006; Thomsen et al., 2000; Weiss et al., 2003a; see also Chapter 15). There is also some evidence that right hemisphere regions are more engaged in spatial tasks than left hemisphere regions, particularly for men (see Section 26.4.3.4).

The brain regions activated by men and women during mental rotations tasks are largely overlapping when there are no sex differences in behavioral performance, but some brain differences have been reported. Women engage portions of the frontal lobe, in particular the right inferior frontal gyrus, that men generally do not (Hugdahl et al., 2006; Jordan et al., 2002; Weiss et al., 2003a). For women, it is the activation of these frontal regions (as well as some temporal and parietal regions) that positively predicts task performance accuracy, whereas activation of parietal regions (e.g., postcentral gyrus and precuneus) positively predicts accuracy for men (Butler et al., 2006). The different patterns of task-related brain activation for women and men might reflect women's use of top-down processing and men's use of bottom-up processing to complete mental rotations tasks (Butler et al., 2006).

Functional brain sex differences during mental rotations tasks when the sexes differ in performance may tell us about the neural substrates of the cognitive difference, although the performance differences may complicate interpretation. Most behavioral tests of mental rotations involve comparisons among multiple figures, whereas most neuroimaging studies of mental rotations involve a pairwise comparison because of scanner space constraints; the sex difference in mental rotations performance is likely reduced in the latter compared to the former (Peters and Battista, 2008). In one fMRI study in which men outperformed women, there were no sex differences in brain regions activated by the task, but women had significantly greater activation of those regions than men (Halari et al., 2006); this is consistent with the notion that increased activation reflects the need to work harder (e.g., Gur et al., 2000).

There are also sex differences in brain activation during other visuospatial tasks. When matching the orientation of angled lines, men were reported to have greater activation than women of left occipital and cingulate regions, and this effect increased with age (Clements et al., 2006; Clements-Stephens et al., 2009); in contrast, no regional brain sex differences were found in a similar task in which a joystick was used to move a cursor in a specified angle away from a central stimulus (Christova et al., 2008). During spatial navigation, men were seen to engage more left temporal regions than women, and women to engage more right frontal, parietal, and hippocampal regions than men (Grön et al., 2000), although sex differences in related tasks have not always been found (Ohnishi et al., 2006). During spatial attention tasks, men appear to activate left parietal regions more than women, whereas women engage more right frontal regions than men (Rubia et al., 2010), although this difference is not always found (Bell et al., 2006). These studies converge to indicate that visuospatial tasks engage different brain systems in the two sexes: men recruit left hemisphere regions to a greater degree than women, and women recruit frontal lobe regions that men generally do not. Unfortunately, it is difficult to review these findings in relation to behavioral performance because of the limited number of studies available and differences across studies in the tasks used.

26.4.3.2 Language

Several studies have focused on finding the neural substrates of the female advantage in verbal ability described in Section 26.2.1.3. Generally, in both sexes, activity in regions of the left hemisphere, including the temporal lobe, prefrontal cortex, inferior frontal gyrus, cingulate, and regions of the parietal lobe is associated with the performance of most language tasks, including verbal fluency, rhyming, and comprehension (Allendorfer et al., 2012; Buckner et al., 1995; Burman et al., 2008; Clements et al., 2006; Frost et al., 1999; Gauthier et al., 2009; Halari et al., 2006; Plante et al., 2006; Shaywitz et al., 1995; Weiss et al., 2003b).

As for spatial ability, findings of sex differences in brain activation for language tasks using fMRI depend upon whether the sexes are matched on behavioral performance. When they are matched on task performance, most studies do not find differences in brain activation (Allendorfer et al., 2012; Clements et al., 2006; Donnelly et al., 2011; Frost et al., 1999; Weiss et al., 2003b). Nonetheless, differences favoring both sexes have also been reported: men have been seen to have greater activation than women in language-related regions (Buckner et al., 1995; Gauthier et al., 2009); the reverse has also been found, with women having greater activation than men, particularly in right hemisphere regions (Plante et al., 2006; Shaywitz et al., 1995). When the sexes are not matched on task performance, women behaviorally outperform and display greater brain activation than men, especially in right hemisphere regions (Burman et al., 2008; Halari et al., 2006; Plante et al., 2006), consistent with other data discussed in Section 26.4.3.4 suggesting

bilateral representation of language in women. (This argument might appear inconsistent with that presented in Section 26.4.3.1, that is, that the greater frontal lobe activity of women during spatial tasks reflected their need to work harder than men. Issues pertaining to the interpretation of sex differences in brain function are complicated, however, as we discuss in Section 26.4.3.6.) Furthermore, the link between performance accuracy and brain activation differs for men and women: in women, accuracy is strongly linked to primary language areas in the bilateral frontal and left temporal lobes; in men, accuracy is weakly linked to primary left hemisphere language regions and also to secondary language areas, such as the left caudate and cingulate and right parietal lobe (Allendorfer et al., 2012; Burman et al., 2008; Donnelly et al., 2011).

26.4.3.3 Emotional Recognition

Much imaging work has concerned the neural substrates of sex differences in the processing of emotions, enough for reviews of sex differences in brain activity during the processing of emotional information, with a focus on amygdala engagement during the viewing of emotional human faces (Fusar-Poli et al., 2009; Sergerie et al., 2008). (It is interesting that most studies on emotion have focused on faces, rather than voices or prosody. See Chapter 18 for further reading on the neurobiology of face processing.) The viewing of emotional faces generally elicits activation in several brain regions, including the amygdala, frontal and prefrontal cortices, anterior cingulate cortex, insula, as well as areas in the temporal, parietal, and occipital lobes (Fusar-Poli et al., 2009; Sergerie et al., 2008). The amygdala is typically engaged in the viewing of all emotions, in particular happy, sad, and fearful faces (Fusar-Poli et al., 2009); this is likely a reflection of its central connectivity to visual, subcortical, and cortical regions of the brain, all of which are engaged in the detection of emotional cues and subsequent planning of behavioral responses (Pessoa and Adolphs, 2010).

There are sex differences in amygdala volume (larger in men than in women) and amygdala activation during the viewing of emotional faces (men have greater activation than do women). Two meta-analyses of over 100 empirical studies each have confirmed the sex differences in brain activation during emotion recognition tasks: men have greater bilateral activity than women in limbic areas, including the amygdala, and in prefrontal regions (Fusar-Poli et al., 2009; Sergerie et al., 2008), perhaps reflecting their need to work harder on the task, since women typically outperform men in the decoding of emotions (Section 26.2.2.4). Task performance was not explicitly considered in the meta-analyses, and studies varied in their measurement and reporting of behavioral sex differences. Few studies have, in fact, investigated sex differences in the link between amygdala

activation and performance on emotion recognition tasks: the frontal lobe inhibits amygdala activation during explicit identification of emotions versus the passive viewing of emotions (Critchley et al., 2000; Hariri et al., 2000), so most emotion recognition tasks do not require explicit behavioral responses. The limited available data suggest that bilateral amygdala activity is positively linked to emotion recognition accuracy for both men and women (Derntl et al., 2009; Habel et al., 2007).

There are also sex differences in amygdala activation during other emotion-related tasks. In a manner consistent with findings on facial emotion recognition, men show more amygdala activity than women during the viewing of sexual stimuli (reviewed in Hamann, 2005). During emotional memory tasks, the amygdala is activated in both sexes, but activation is greater in the left amygdala in women and in the right amygdala in men. This finding is not easy to interpret, but it has been suggested that sex differences in internalizing psychopathology arise in part through differences in memory for the gist of (right hemisphere) versus the details of (left hemisphere) negative emotional episodes (reviewed in Cahill, 2010; Hamann, 2005) (See Chapter 16 for further reading on the neurobiology of memory development.) Compared to emotional memory tasks, which emphasize emotions with a negative valence and have dominated the literature, tasks that emphasize emotions with a positive valence elicit different patterns of brain sex differences, with women showing more frontal and temporal activity than men, and men showing more left amygdala activity than women (Stevens and Hamann, 2012).

26.4.3.4 Lateralized Functions

Lateralization, also referred to as hemispheric specialization or functional asymmetry, has been a popular explanation for cognitive sex differences, particularly for language and spatial abilities. Typically, the left hemisphere, which houses both Broca's and Wernicke's areas, is dominant for sequential processing, including language, and the right hemisphere is dominant for simultaneous processing, including spatial abilities (for reviews, see Bryden, 1982; Hall et al., 2008; Kansaku and Kitazawa, 2001; Kimura, 1999). Data going back several decades, derived from patients with brain damage and behavioral tasks in typical individuals (such as split-field visual tasks, dichotic listening, and electroencephalogram asymmetry), suggest that women are less lateralized than men, especially for language (Bryden, 1982; McGlone, 1980). The topic has also been studied using fMRI, but results are often task- and method-dependent and subject to misinterpretation. For example, evidence reviewed above suggests that women have more right hemisphere activation than men for language tasks, and men have more left hemisphere activation than women for spatial tasks, but this does not mean that men are left-lateralized for

language and women are right-lateralized for spatial tasks. Lateralization must be explicitly tested by comparing activation in the two hemispheres; it is not sufficient to show that the activity of only one hemisphere is above baseline or that there are significant sex differences in specific regions of a single hemisphere. When the correct analyses are conducted, women show less lateralization than men. Women's reduced lateralization has been suggested to be linked to greater interhemispheric communication facilitated by their larger interhemispheric commissures (e.g., CC and anterior commissure) (Halpern, 2012; Hines et al., 1992).

There is some evidence for sex differences in functional lateralization of spatial ability, although findings from neuroimaging (PET and fMRI) are not always consistent with those from perceptual asymmetry assessments (e.g., split visual field and dichotic listening tasks), suggesting that the methods are measuring different aspects of lateralization. A meta-analysis of sex differences in lateralization of spatial tasks measured by a variety of methods (e.g., fMRI, PET, split visual field, brain damage) found that men primarily engage the right hemisphere and women engage both hemispheres when solving spatial tasks (Vogel et al., 2003). However, the findings from the fMRI studies on spatial ability reviewed above (Section 26.4.2.1) in which lateralization was explicitly examined are mixed: some reported greater right than left hemisphere activity for both men and women (Halari et al., 2006; Hugdahl et al., 2006), others reported more right-lateralized activity in men than women (e.g., Christova et al., 2008) or in women than men (e.g., Clements et al., 2006), and still others reported no lateralization effects (e.g., Weiss et al., 2003a).

Women have somewhat greater bilateral representation for language than men. Two recent meta-analyses of fMRI and PET studies on language lateralization reported weak support for left-lateralization in men but not women in several domains (Sommer et al., 2004, 2008), and meta-analyses using other behavioral methods (e.g., dichotic listening) reveal similar differences (Bryden, 1982; Sommer et al., 2008; Voyer, 2011). Findings from the fMRI studies on language reviewed above (Section 26.4.3.2) are consistent with these meta-analyses, with some reporting greater left than right hemisphere activity in both sexes (Frost et al., 1999; Plante et al., 2006; Weiss et al., 2003b), and others reporting this effect only for men (Clements et al., 2006; Shaywitz et al., 1995).

Sex differences in amygdala lateralization during emotion-related tasks are task-dependent. Studies on emotion recognition reviewed above (Section 26.4.3.3), in which task performance and lateralization effects were explicitly examined, found no support for sex differences (Derntl et al., 2009; Habel et al., 2007). This bilateral pattern of activation may depend on development, though: recent work shows right-lateralized amygdala

activity during facial emotion recognition for adolescent boys (but not girls) (Schneider et al., 2011). There is also evidence for sex differences in amygdala lateralization during other emotion tasks in adults: men have right-lateralized and women have left-lateralized amygdala activity for emotion-related memories (Cahill, 2010; Hamann, 2005). A meta-analysis of fMRI and PET studies on a combination of emotion-related tasks found that men had more right-lateralized activity than women (Wager et al., 2003), but other work suggests that sex differences disappear with improved meta-analytic methodology (e.g., incorporating effect sizes of original findings into the analysis) (Sergerie et al., 2008).

There are few studies directly examining the link between sex differences in lateralized activation and sex differences in cognitive performance. For spatial ability, greater (usually right) lateralization is thought to be linked to better performance because the processing of spatial information is unhindered by language circuitry. For language, the lateralization-performance link is unclear: greater lateralization has been associated with poorer language skills in typical males (compared to females), and incomplete lateralization has been hypothesized to be a risk factor for language disorders (Hall et al., 2008). Interestingly, the limited data on the association between lateralization and performance concern language tasks. As expected, results are largely inconsistent, likely due to study variations in task designs and the poor temporal resolution of PET and fMRI – a general limitation of the techniques that is particularly critical in examinations of the speed and timing of interhemispheric processing (for discussion, see Hall et al., 2008; Kansaku and Kitazawa, 2001; Kitazawa and Kansaku, 2005; Ortigue et al., 2005). It is important to note that rarely are women reported to be more lateralized than men, so inconsistencies likely reflect differential measurement sensitivity and small sex differences. Given the relatively small sex differences in brain lateralization and the relatively large sex differences in some abilities, it is very unlikely that lateralization differences completely account for cognitive sex differences.

26.4.3.5 Development of Sex Differences in Brain Function

There are fewer studies of functional brain development than structural brain development, although structure and function are certainly interdependent. Typically, brain activity related to cognitive task performance becomes less diffuse and more fine-tuned with age, probably related to increasing connectivity among brain regions (Casey et al., 2005; Giorgio et al., 2008). For example, brain function in children is driven by short-range connections among anatomically close regions; in adults, many local connections are replaced

by long-range ones, reflecting greater neural integration with development (Fair et al., 2007, 2009).

Brain function in adolescence is likely affected by the different trajectories of gray and white matter development, and these brain changes may underlie the increased risk-taking behavior characteristic of this developmental period. Limbic regions, which are implicated in affective processing, mature in early-to-mid adolescence, whereas the prefrontal cortex, which is thought to subserve cognitive control functions, is among the last brain region to undergo cortical thinning and myelination. The discordant maturational timing between these affective and cognitive neural processing networks is thought to result in limited top-down control of responses to appetitive stimuli such as peers and addictive substances (Casey et al., 2011; Steinberg, 2008). Because girls have faster brain development compared to boys, they are thought to experience a shorter period of discordance between limbic and prefrontal regions and therefore to be less likely to engage in the type of risk-taking behavior that emerges in adolescence (e.g., risky sex, substance use).

26.4.3.6 Implications of Sex Differences in Brain Function

There are several conclusions that emerge from the studies reviewed; a simplified summary of sex differences in neural activation to spatial, language, and emotion-related tasks is provided in Figure 26.4. First, with respect to visuospatial tasks, particularly mental rotations, both men and women engage parietal regions, but women engage frontal regions that men typically do not, and men engage some left-hemisphere regions that women typically do not (Figure 26.4(a)). Second, with respect to language tasks, women recruit more bilateral frontal and temporal regions than do men (Figure 26.4(b)). Third, with respect to the processing of emotional faces, men show greater bilateral amygdala activity than do women (Figure 26.4(c), right), perhaps reflecting their need to work harder than women to decode emotions. Fourth, with respect to negative emotional memory, women show greater left amygdala activity than men, and men show greater right amygdala activity than women (Figure 26.4(c), left); this difference is considered to have implications for sex differences in psychopathology (Cahill, 2010; Hamann, 2005; Stevens and Hamann, 2012).

We can also draw some general conclusions regarding sex differences in the lateralization of brain function for cognition and the link between brain activation and performance on cognitive tasks. With respect to lateralization, although the evidence is mixed, it appears that women are more likely than men to process material in both hemispheres; the lateralized activity of men appears to contribute to some cognitive advantages (e.g., in spatial ability) and disadvantages (e.g. in language).

With respect to brain activation–task performance links, performance accuracy is associated with activation of different brain regions for men and women for both visuospatial and language tasks, perhaps reflecting the use of sex-specific strategies.

Thus, the sexes engage similar brain regions to solve cognitive tasks, but they also appear to diverge in some notable ways. The sex differences primarily reflect two brain processes: efficiency and integration. Greater brain activity in the sex that typically performs worse on a behavioral task than the sex that performs better can be understood in terms of neural efficiency. When performance is poor, the task is seen to be difficult, and thus more neural resources are recruited to solve it. This interpretation is consistent with findings from studies in which task difficulty was manipulated: the neural substrates of a task become more widely distributed as task difficulty increases (e.g., Gur et al., 2000). Greater brain activity in the sex that typically performs better on a behavioral task than the sex that performs worse can be understood in terms of neural integration. When performance is good, the task elicits a diverse set of associations, subserved by greater neural engagement. This interpretation is consistent with findings on the neural systems underlying intelligence: functional connectivity among brain regions is positively associated with intelligence (Song et al., 2008). Whether efficiency or integration is invoked as an explanation for functional brain sex differences is likely dependent upon the nature of the task (e.g., complexity) and methodology (e.g., sample characteristics, task design, data analysis procedures); they are not mutually exclusive explanations, as evidenced by recent work on the efficiency of small-world networks (Fair et al., 2009; Sporns, 2011).

It is important to note that evidence regarding sex differences in brain function during performance of spatial, language, and emotion-related tasks is not completely consistent, for several reasons. First, results regarding sex differences in brain activation depend upon whether or not sex differences in task performance occurred and how they were considered. Second, samples are small in many neuroimaging studies, leading to low statistical power (and difficulty in detecting sex differences). Third, tasks and stimulus presentation methods vary across studies, so brain activation patterns are difficult to compare across studies. Fourth, participants vary across studies in sample characteristics, such as age; given sex differences in developmental trajectories (McClure et al., 2004; Plante et al., 2006; Rubia et al., 2010), it is important to be sure that findings reflect sex rather than developmental status. Fifth, the scanning environment constrains behavioral assessments in several ways (e.g., space, stimulus presentation), so the behavior measured in the scanner likely differs from the behavior that shows a sex difference outside the scanner (e.g., Peters and Battista, 2008).
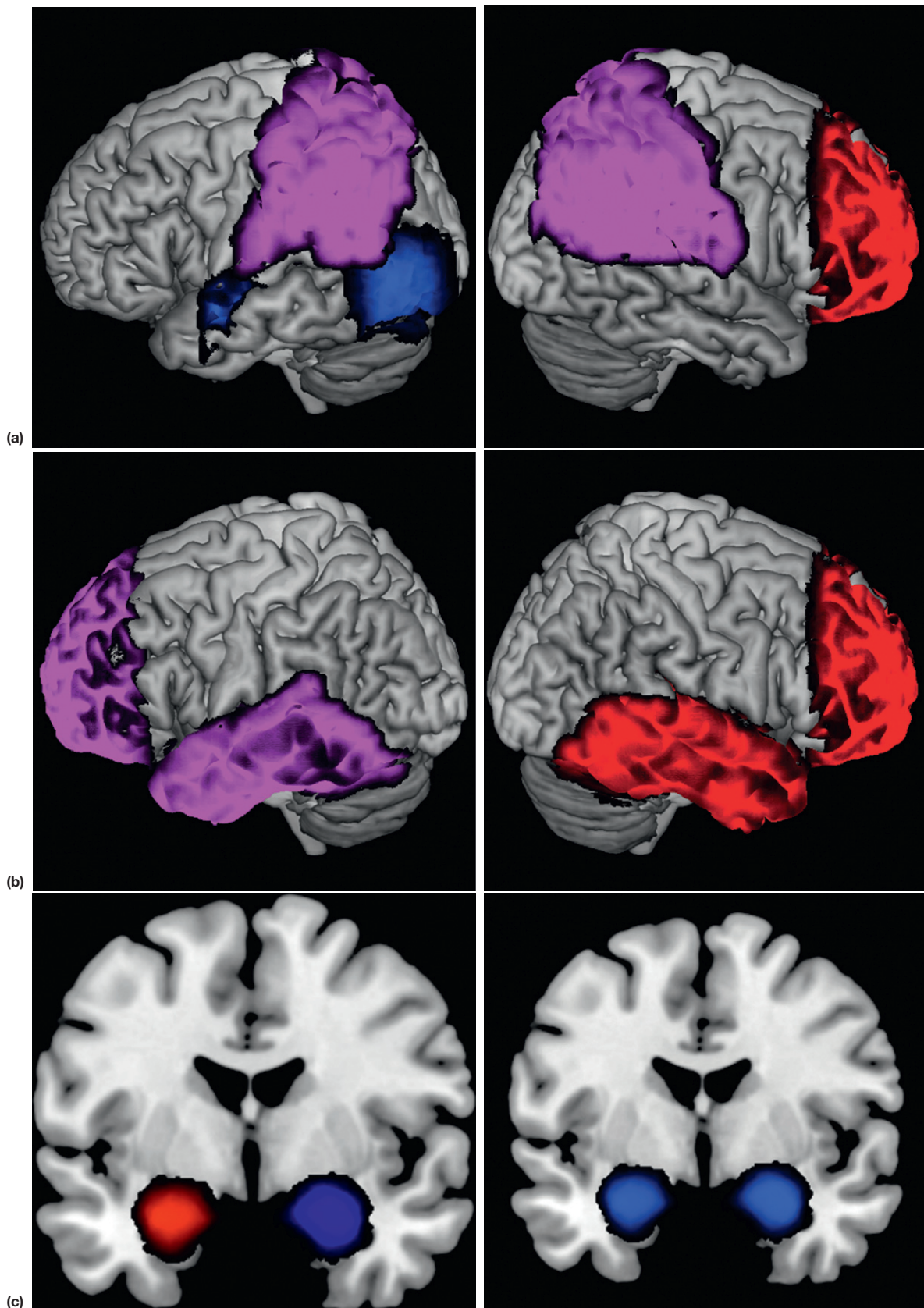
FIGURE 26.4   Summary of sex differences in neural activation to sex-typed tasks. Colors indicate areas of brain activation: Men in blue, women in red, overlap in purple. (a) Spatial tasks; right: right hemisphere, left: left hemisphere. (b) Language tasks; right: right hemisphere, left: left hemisphere. (c) Amygdala during emotion-related tasks depicted on coronal slice; right: facial recognition, left: emotional memories (see text for details).

26.5 CAUSES OF BRAIN SEX DIFFERENCES

The brain is plastic, and its development is influenced by a combination of genetic, epigenetic, hormonal, and experiential effects throughout the lifespan. Most aspects of brain development reflect a dynamic interplay among these factors and are therefore difficult to isolate and investigate (Cosgrove et al., 2007; McCarthy and Arnold, 2011; Poldrack, 2000).

Animal models are important for informing examinations of human neural processes. Many brain regions that show sex differences in human beings correspond to sexually dimorphic brain regions in nonhuman animals (Goldstein et al., 2001), and animal studies have helped to guide many human studies; however, the degree to which animal findings generalize to human beings is not always clear, particularly with respect to cognitive domains that are species-specific, such as language.

Research on the causes of human brain sex differences is relatively new; thus, the studies we review below must be interpreted critically and require replication. Parallel to our discussion of the causes of psychological sex differences (Section 26.3), we consider influences on brain sex differences of socialization, genes, and focus on hormones (prenatal, adolescent, and circulating).

26.5.1 Socialization Contributions to Brain Sex Differences

Brain sex differences are usually considered to be innate, but the brain changes in response to experiences, so it is important to consider socialization (Cosgrove et al., 2007). Although sex-differential experiences were not measured in most studies reviewed above (Section 26.4), socialization effects could account for variability in findings and inconsistencies across reports. For example, studies failing to find sex differences in white matter volume (as discussed in Section 26.4.2.4) could reflect effects of sex-differential experiences; perhaps certain male-typed experiences (e.g., engaging in spatial activities) facilitate white matter growth, so girls who have these experiences have more 'male-typical' white matter than girls who do not have these experiences.

There is much interesting work to be done regarding socialization influences on brain sex differences, particularly examining the ways in which training on cognitive tasks might differentially mediate (or be mediated by) brain sex differences. For example, we suggest above (Section 26.4.3.1) that sex differences in brain activation during the performance of spatial tasks might reflect sex-differential strategy use during task completion (see also Butler et al., 2006; Clements-Stephens et al., 2009; Jordan et al., 2002; Thomsen et al., 2000). We also review above evidence for the potential elimination of the behavioral sex difference in spatial tasks through training (Section 26.3.1.2). Thus, the sex difference in brain activation during spatial task performance might be partially explained by sex-differential experiences with spatial stimuli, and consequently, learned strategies for manipulation of those stimuli. Investigations of cognitive training effects on brain function of males and females are warranted.

26.5.2 Genetic Contributions to Brain Sex Differences

There is little conclusive evidence regarding sex chromosome contributions to human brain development and the ways in which genes and the environment interact to influence the brain in sex-differential ways. Recent twin data show greater genetic influences on white matter development in boys than girls (Chiang et al., 2011). Consistent with this, intriguing preliminary evidence indicates that several genes on the Y chromosome are expressed in the human male prenatal brain at midgestation (Reinius and Jazin, 2009) and the adult male brain (Vawter et al., 2004); however, development of the external genitalia is underway by midgestation and complete maturation has occurred by adulthood, so these findings might also reflect hormone (e.g., androgens from the testes) or experiential effects on the brain.

Some insight into the role of the X chromosome in brain sex differences is also provided by studies of girls and women with Turner syndrome (TS), who have a single (X) sex chromosome. Compared to unaffected controls, girls and women with TS have decreased parietal lobe volume and decreased activation in parietal lobe regions during a variety of visuospatial tasks; they also have increased amygdala volume and increased amygdala activation during the recognition of fearful faces. These findings are consistent with their cognitive profile, which is characterized, in part, by visuospatial and emotion recognition deficits (reviewed in Knickmeyer and Davenport, 2011). The implications of these findings for brain sex differences in the unaffected population are unclear for several reasons. First, brain differences are confounded by cognitive performance differences: TS and unaffected control groups generally differ on task performance in functional imaging studies. Second, sex hormone production is low in individuals with TS; thus, differential patterns of brain structure and function in individuals with TS as compared to those in unaffected girls and women might reflect sex hormone influences instead of X-chromosome influences on the brain. This is consistent with evidence showing that estradiol

replacement in adolescents with TS reduces differences between girls with TS and control girls (Lepage et al., 2012). Third, it is unclear whether findings in individuals with TS reflect effects of the X chromosome, having a single (be it X or Y) sex chromosome, or X-chromosome dosage. Effects of X-chromosome dosage have been investigated by comparing brain structure in men with Klinefelter Syndrome (XXY) to unaffected men and women. Unfortunately, results from these studies are not easy to interpret because (as in studies in women with TS) X-dosage effects are confounded with effects of sex hormones (for discussion, see Bryant et al., 2011; Lentini et al., 2012). There is clearly much opportunity for future work on sex chromosome influences on brain sex differences.

26.5.3 Hormonal Contributions to Brain Sex Differences

Sex hormones, particularly androgens, are the most investigated cause of sex differences in the human brain. There is evidence from clinical and typical samples for prenatal, adolescent, and circulating sex hormone influences on the brain, but this research area is relatively new, and conclusions must be tentative.

26.5.3.1 Prenatal Hormone Links to Brain Sex Differences

The influence of androgens present during early development on structural brain sex differences has been examined in individuals with CAH and in typical boys whose amniotic testosterone levels were assessed. As discussed above (Section 26.3.4), androgens masculinize a variety of characteristics in girls and women with CAH (including activity interests, some social behaviors, and spatial ability). Structural imaging studies reveal effects that are generally more consistent with the disease process than with prenatal hormone effects on the brain; smaller amygdala volumes were reported in both males and females with CAH than in unaffected males and females (Merke et al., 2003), likely reflecting effects of postnatal cortisone treatment in individuals with CAH. In typical boys aged 8 to 11 years, testosterone levels from amniotic fluid have been linked to gray matter volumes in brain regions that show sex differences. Specifically, testosterone was positively linked to gray matter volumes in temporal regions, but negatively linked to volumes in occipital and frontal regions (Lombardo et al., 2012). More research is necessary to determine if this pattern of results is also seen in girls and if it changes with development.

Findings regarding prenatal androgen influences on brain function suggest altered amygdala and hippocampal activity in individuals with CAH, but interpretation is not straightforward. Consider findings from one set of studies in which images of emotional faces were viewed, rated, and recalled (Ernst et al., 2007; Mazzone et al., 2011). Brain activation findings showed that girls with CAH had greater amygdala activation while viewing negative facial emotions and less hippocampal activation while recalling emotional faces compared to unaffected girls; however, there were also group differences in behavioral ratings and task performance, complicating interpretation of brain activation differences. In a separate PET functional imaging study, women with CAH were not seen to differ from unaffected women in their neural response to olfactory stimuli: both groups displayed increased amygdala activation to a masculine pheromone and increased hypothalamus activation to a feminine pheromone, compared to men who showed the reciprocal pattern of brain activity (Ciumas et al., 2009).

Information about prenatal androgen effects on brain function also comes from typical samples, in which testosterone levels have been measured in amniotic fluid and linked to performance on dichotic listening tasks in childhood. Amniotic testosterone levels were positively associated with left-lateralized language processing in one sample of 6-year-old girls and boys (Lust et al., 2010) and another sample of 10-year-old girls (Grimshaw et al., 1995a). This is consistent with the sex difference in language lateralization reported in adults and children (Section 26.4.3.4). Amniotic testosterone levels have also been associated with right-lateralized emotion processing (measured with an emotion–word dichotic listening task) in 10-year-old boys (Grimshaw et al., 1995a), consistent with meta-analytic findings on right-lateralized amygdala activation in men (but not women) during emotion-related tasks (Wager et al., 2003).

26.5.3.2 Adolescent Hormone Links to Brain Sex Differences

There is considerable interest in the ways that brain changes in adolescence reflect the direct effects of pubertal sex hormones, although most work has not been able to differentiate permanent (organizational) effects of hormones from transient (activational) effects. Generally, pubertal increases in sex-specific gonadal hormones (estrogen in girls and testosterone in boys) are associated with decreases in cortical gray matter volume (reviewed in Peper et al., 2011). When boys and girls are matched on pubertal development, however, sex differences in links between testosterone and regional gray matter volumes are more difficult to interpret, with boys showing fewer significant associations than girls (Bramen et al., 2012). This apparent discrepancy may be explained by androgen sensitivity. The efficiency of the androgen receptor gene has been suggested to moderate the influence of sex hormones on cortical thinning: fewer repeats

of a functional polymorphism within the gene predicted more 'masculinized' patterns of maturation (Paus et al., 2010; Raznahan et al., 2010).

There is stronger evidence for a link between pubertal hormones and white matter development in boys than in girls. In boys, increases in testosterone at puberty have been linked to increases in white matter volume (reviewed in Peper et al., 2011), with the efficiency of the androgen receptor gene moderating this association (Paus et al., 2010; Perrin et al., 2008). Testosterone levels – but not pubertal stage – have also been linked to FA increases in boys (Bava et al., 2011; Herting et al., 2012). Findings are inconsistent for girls: advanced pubertal stage has been positively linked to increases in white matter volume (Peper et al., 2011), but estradiol levels have been negatively associated with FA in girls (Herting et al., 2012). Differences in brain links with hormone levels versus pubertal stage may reflect limitations in self-reports of pubertal stage for both sexes (discussed in Dorn et al., 2006).

Pubertal hormone effects on brain function have been studied less than effects on brain structure, but some insight is provided by a study on the neural substrates of a monetary reward task (Forbes et al., 2010). Girls and boys with more advanced pubertal development (compared to same-age peers with less advanced development) showed less striatum and more prefrontal cortex activation at reward *presentation*, consistent with evidence for the discordant maturation of affective and cognitive neural processing networks in adolescence (Section 26.4.3.5). For boys only, testosterone levels were positively linked with striatum activity during reward *anticipation*, perhaps reflecting a sex difference in the neural substrates of consummatory anticipation that emerges at puberty. Estradiol links to brain function were not examined in this study, presumably because the measurement of this hormone is problematic, particularly during puberty (Dorn and Biro, 2011).

The influence of pubertal hormones on brain sex differences has also been investigated in boys with extremely early (disordered) puberty (Mueller et al., 2009, 2011a,b). Results are difficult to interpret, however, because of age and performance differences between clinical and control groups. Nonetheless, this research illustrates a valuable approach (i.e., neuroimaging individuals with atypical pubertal timing) to understanding hormonal influences on brain development.

26.5.3.3 Circulating Hormone Links to Brain Sex Differences

Relations between regional volumes and circulating hormone levels in adults provide evidence for transient (activational) effects of sex hormones on sex-related brain structure, as seen in both clinical and typical samples. Changes in overall brain volume were observed in a sample of transsexuals after 4 months of hormone treatment (antiandrogens + estrogens for male-to-female, and androgens for female-to-male) (Hulshoff Pol et al., 2006). Compared to untreated controls, male-to-female transsexuals showed decreases in overall brain volume, and female-to-male transsexuals showed increases in overall brain and hypothalamus volumes. These findings are consistent with the sex differences reported above (Sections 26.4.2.1. and 26.4.2.2.3) and suggest that androgens increase overall and some regional brain volumes. Nonetheless, the results regarding circulating androgen influences on overall brain volume are surprising, given that the sex difference in brain volume is apparent in childhood (Section 26.4.2.1). Regional specificity of hormone effects has been seen in samples of typical adults, but results differ across studies, likely due to differences in sample characteristics (e.g., age) and methods (e.g., how sex differences were accounted for in brain-hormone links). Circulating estrogen levels were positively linked to gray matter volume in the left superior parietal gyrus, but results differ across studies, likely due to differences in sample characteristics (e.g., age) and methods (e.g., how sex differences were accounted for in brain-hormone links). Circulating testosterone levels were negatively linked to gray matter volume in the left inferior frontal gyrus (Witte et al., 2010) and positively linked to gray matter volumes in the hippocampus, amygdala, insula, and occiptial regions (Lentini et al., 2012)

Examinations of structural and functional brain changes at menopause and during different phases of the menstrual cycle provide indirect evidence for activational effects of estrogens on the brain. Generally, the hippocampus and frontal lobes are implicated as the primary sites for estrogen effects on brain structure in humans; thus, estrogen effects on brain function are most evident in verbal memory tasks, which show a sex difference that favors females (Section 26.2.1.4), and are subserved by the hippocampus and frontal lobes (Maki, 2005; Maki and Resnick, 2001). At menopause, there is evidence for decreases in whole brain, frontal lobe, and hippocampal volumes (Goto et al., 2011; Robertson et al., 2009). Further, estrogen therapy begun around the onset of menopause and of a relatively short duration (about 5 years) offsets these volume reductions (Erickson et al., 2010; Lord et al., 2008; Resnick et al., 2009). Postmenopausal women undergoing estrogen therapy have also been shown to have greater activation of frontal, parietal, and hippocampal regions during verbal and working memory tasks in comparison to postmenopausal women who never used estrogen therapy (Berent-Spillson et al., 2010; Dumas et al., 2010; Persad et al., 2009; Shaywitz et al., 1999). Interestingly, the increased activation with hormone therapy did not predict

better memory in these studies; there were no performance differences between estrogen therapy users and nonusers on the memory tasks. Estrogen therapy users, however, had greater cerebral blood flow and better memory task performance than nonusers in research using PET; thus, cerebral blow flood may be one mechanism through which estrogen influences cognition (and is best measured by PET; Maki and Resnick, 2000; Resnick et al., 1998). This is a promising area for future research.

Indirect evidence for estrogen influences on the structure and function of the brain is also provided by research with women at different phases of their menstrual cycle. In high-estrogen phases of the menstrual cycle as compared to low-estrogen phases, women generally show more hippocampal volume as well as left frontal and temporal activation during the completion of verbal and mental rotation tasks (Dietrich et al., 2001; Fernández et al., 2003; Konrad et al., 2008; Protopopescu et al., 2008; Schöning et al., 2007). As with findings from studies on estrogen therapy at menopause, the implications of this research are not clear, because there is currently little evidence for a relation between estrogen-influenced brain activation and task performance: in the functional studies reviewed above, increased left frontal lobe activation in the high-estrogen phase of the cycle did not predict differential task performance (Dietrich et al., 2001; Fernández et al., 2003; Konrad et al., 2008). Similarly, during the high-estrogen phase of the menstrual cycle as compared to the low-estrogen phase, estradiol levels predicted greater left frontal lobe activation during a verbal memory task, but they did not predict better task performance (Craig et al., 2008).

In summary, there is little conclusive evidence regarding social, genetic, or hormonal contributions to sex differences in human brain structure and function, but this research area is growing. Most of the available data concern hormones. Preliminary findings suggest that prenatal androgen influences the activity of the hippocampus, amygdala, and lateralization of the brain for language- and emotion-related tasks. There is also some indication that sex-specific hormones at puberty are linked to the reduction of gray matter volume in adolescence, and that testosterone in boys is linked to the adolescent increase in white matter. Finally, there is evidence for activational effects of sex hormones on the adult brain, particularly for estrogen influences on hippocampal and frontal lobe function. Unfortunately, there are few data linking sex hormone influences on the brain with behavior. There are also few data regarding sex chromosome expression in the human brain, and no data regarding socialization influences on brain sex differences. Thus, there is much opportunity for future research.

26.6 CONCLUSIONS AND FUTURE DIRECTIONS

As reviewed above, the sexes differ in significant ways in both behavior and the brain (including structure and function), although there is still much to be learned regarding sex differences and their development and causes. It is important to be aware of the ways in which age and sample size can affect conclusions regarding the existence – or not – of sex differences.

There is good evidence that both sex hormones and social factors influence the development of human sex-related psychological characteristics, although little is currently known about the pathways by which socialization acts on and modifies biological predispositions. Determinants of brain sex differences are still largely unknown, but it is important to remember that the brain is plastic and that sex differences likely emerge from the interplay of genes, sex hormones, and social experiences. Brain sex differences cannot be assumed to be innate.

There are several opportunities to study the etiology of sex differences in brain and behavior. First, sex differences in early brain development can be studied in natural experiments in which prenatal hormone exposure is sex-atypical, such as CAH. These conditions help us to separate the relative influences of early (prenatal and neonatal) hormones and postnatal socialization, and, more important, allow the study of their interplay. Examples of the information that can be gained from these conditions have been reviewed in this chapter and elsewhere (Berenbaum and Beltz, 2011; Blakemore et al., 2009). Second, sex differences in adolescent brain development can be studied in individuals with disordered pubertal development. This provides an opportunity to test hypotheses about permanent changes to the brain induced by sex hormones (Sisk and Zehr, 2005, reviewed in Berenbaum and Beltz, 2011; Giedd et al., 2006). Third, sex differences in adolescent brain development can also be studied in typical individuals, by linking variations in pubertal development to changes in behavior and in the brain. There is some intriguing recent cross-sectional work in this area (reviewed in Berenbaum and Beltz, 2011; Peper et al., 2011), but longitudinal studies are optimal for learning how hormones and socialization at puberty influence brain changes and for examining the permanence of the changes.

The links between neural and behavioral sex differences are beginning to be understood, but they must be directly tested. It is not sufficient to find sex differences in regions of the brain known to subserve specific sex-related behavioral characteristics; sex differences in those regions of the brain must be shown to *explain* the behavioral sex differences.

There are several opportunities to understand direct links between sex differences in the brain and behavior. First, the meaning of sex differences in brain activation – when they reflect strategy use (when the sexes perform similarly) or behavioral differences (when the sexes differ in performance) – can be understood by manipulating task difficulty during functional brain scanning. Such types of designs are rare in examinations of sex differences, but they are typical in other research areas (e.g., Poldrack, 2000). Second, causal inferences about links between brain and behavior can be strengthened by using effective connectivity mapping which takes advantage of the time series nature of functional neuroimaging data. Work on functional and structural connectivity reviewed in this chapter has identified brain regions with related functional activity (e.g., Fair et al., 2007, 2009) and structural connections (e.g., Schmithorst and Yuan, 2010), but effective connectivity mapping would allow prediction of regional brain activity from activity in other brain regions or task performance (e.g., Gates et al., 2010, 2011; Kim et al., 2007). For example, effective connectivity mapping enables inferences regarding the direction of a connection between two brain regions: the connection might go from region A to region B for women, but from region B to region A for men. Third, neural effects of sex-differential experiences can be studied using longitudinal neuroimaging designs. For example, studies of cognitive training effects on changes in brain structure or function can reveal the plasticity of the brain and indicate how sex differences arise and how they might be modified (and the within-subject design avoids the confounding influence of sex differences in brain size) (e.g., Thambisetty et al., 2010).

In sum, the sexes are similar in many ways, but there are notable differences in their brain and behavior (including cognitive abilities). An understanding of sex differences has implications for discussions about women's underrepresentation in science and mathematics careers as well as for the differences in the etiology, appearance, and treatment of psychopathology between boys and men as compared to girls and women. Studying sex differences can also tell us about individual differences generally. By identifying the differences, delineating their development, and investigating their causes, we begin to uncover the mechanisms underlying variation in human health, disease, and behavior.

References

Allen, L.S., Gorski, R.A., 1990. Sex difference in the bed nucleus of the stria terminalis of the human brain. The Journal of Comparative Neurology 302, 697–706.

Allen, L.S., Gorski, R.A., 1991. Sexual dimorphism of the anterior commissure and massa intermedia of the human brain. The Journal of Comparative Neurology 312, 97–104.

Allen, L.S., Gorski, R.A., 1992. Sexual orientation and the size of the anterior commissure in the human brain. Proceedings of the National Academy of Sciences of the United States of America 89, 7199–7202.

Allen, J.S., Damasio, H., Grabowski, T.J., Bruss, J., Zhang, W., 2003. Sexual dimorphism and asymmetries in the gray-white composition of the human cerebrum. NeuroImage 18, 880–894.

Allendorfer, J.B., Lindsell, C.J., Siegel, M., et al., 2012. Females and males are highly similar in language performance and cortical activation patterns during verb generation. Cortex 48, 1218–1233.

Archer, J., 2004. Sex differences in aggression in real-world settings: A meta-analytic review. Review of General Psychology 8, 291–322.

Arnold, A.P., 2009. The organizational–activational hypothesis as the foundation for a unified theory of sexual differentiation of all mammalian tissues. Hormones and Behavior 55, 570–578.

Arnold, A.P., Breedlove, S.M., 1985. Organizational and activational effects of sex steroids on brain and behavior: A reanalysis. Hormones and Behavior 19, 469–498.

Arnold, A.P., Chen, X., 2009. What does the 'four core genotypes' mouse model tell us about sex differences in the brain and other tissues? Frontiers in Neuroendocrinology 30, 1–9.

Auyeung, B., Baron-Cohen, S., Ashwin, E., et al., 2009. Fetal testosterone predicts sexually differentiated childhood behavior in girls and in boys. Psychological Science 20, 144–148.

Baenninger, M., Newcombe, N., 1989. The role of experience in spatial test performance: A meta-anaylsis. Sex Roles 20, 327–344.

Baron-Cohen, S., Lutchmaya, S., Knickmeyer, R., 2004. Prenatal Testosterone in Mind. MIT Press, Cambridge, MA.

Bauer, P., 2013. Memory development. Neural Circuit Development and Function in the Healthy and Diseased Brain: Comprehensive Developmental Neuroscience, Volume 3. Elsevier, Oxford.

Bava, S., Boucquey, V., Goldenberg, D., et al., 2011. Sex differences in adolescent white matter architecture. Brain Research 1375, 41–48.

Beck, D.M., 2010. The appeal of the brain in the popular press. Perspectives on Psychological Science 5, 762–766.

Becker, J.B., Breedlove, S.M., Crews, D., McCarthy, M.M. (Eds.), 2002. Behavioral Endocrinology. MIT Press, Cambridge, MA.

Becker, J.B., Berkley, K.J., Geary, N., Hampson, E., Herman, J., Young, E. (Eds.), 2008. Sex Differences in the Brain: From Genes to Behavior. Oxford University Press, New York.

Bell, E.C., Willson, M.C., Wilman, A.H., Dave, S., Silverstone, P.H., 2006. Males and females differ in brain activation during cognitive tasks. NeuroImage 30, 529–538.

Beltz, A.M., Swanson, J.L., Berenbaum, S.A., 2011. Gendered occupational interests: Prenatal androgen effects on psychological orientation to things versus people. Hormones and Behavior 60, 313–317.

Berenbaum, S.A., 2006. Psychological outcome in children with disorders of sex development: Implications for treatment and understanding typical development. Annual Review of Sex Research 17, 1–38.

Berenbaum, S.A., Beltz, A.M., 2011. Sexual differentiation of human behavior: Effects of prenatal and pubertal organizational hormones. Frontiers in Neuroendocrinology 32, 183–200.

Berenbaum, S.A., Baxter, L., Seidenberg, M., Hermann, B., 1997. Role of the hippocampus in sex differences in verbal memory: Memory outcome following left anterior temporal lobectomy. Neuropsychology 11, 585–591.

Berenbaum, S.A., Blakemore, J.E.O., Beltz, A.M., 2011. A role for biology in gender-related behavior. Sex Roles 64, 804–825.

Berenbaum, S.A., Bryk, K.L.K., Beltz, A.M., 2012. Early androgen effects on spatial and mechanical abilities: Evidence from congenital adrenal hyperplasia. Behavioral Neuroscience 126, 86–96.

Berent-Spillson, A., Persad, C.C., Love, T., et al., 2010. Early menopausal hormone use influences brain regions used for visual working memory. Menopause 17, 692–699.

Bishop, K.M., Wahlsten, D., 1997. Sex differences in the human corpus callosum: Myth or reality? Neuroscience and Biobehavioral Reviews 21, 581–601.

Blakemore, J.E.O., Berenbaum, S.A., Liben, L.S., 2009. Gender Development. Psychology Press/Taylor & Francis, New York.

Bornstein, M.H., Hahn, C.-S., Haynes, O.M., 2004. Specific and general language performance across early childhood: Stability and gender considerations. First Language 24, 267–304.

Bramen, J.E., Hranilovich, J.A., Dahl, R.E., et al., 2012. Sex matters during adolescence: Testosterone-related cortical thickness maturation differs between boys and girls. PloS One 7, e33850.

Brun, C.C., Leporé, N., Luders, E., et al., 2009. Sex differences in brain structure in auditory and cingulate regions. NeuroReport 20, 930–935.

Bryant, D.M., Hoeft, F., Lai, S., et al., 2011. Neuroanatomical phenotype of Klinefelter Syndrome in childhood: A voxel-based morphometry study. Journal of Neuroscience 31, 6654–6660.

Bryden, M.P., 1982. Laterality: Functional Asymmetry in the Intact Brain. Academic Press, New York.

Buchanan, C.M., Eccles, J.S., Becker, J.B., 1992. Are adolescents the victims of raging hormones: Evidence for activational effects of hormones on moods and behavior at adolescence. Psychological Bulletin 111, 62–107.

Buckner, R.L., Raichle, M.E., Petersen, S.E., 1995. Dissociation of human prefrontal cortical areas across different speech production tasks and gender groups. Journal of Neurophysiology 74, 2163–2173.

Burman, D.D., Bitan, T., Booth, J.R., 2008. Sex differences in neural processing of language among children. Neuropsychologia 46, 1349–1362.

Burns, N.R., Nettelbeck, T., 2005. Inspection time and speed of processing: Sex differences on perceptual speed but not it. Personality and Individual Differences 39, 439–446.

Butler, T., Imperato-McGinley, J., Pan, H., et al., 2006. Sex differences in mental rotation: Top-down versus bottom-up processing. NeuroImage 32, 445–456.

Byrnes, J.P., Miller, D.C., Schafer, W.D., 1999. Gender differences in risk taking: A meta-analysis. Psychological Bulletin 125, 367–383.

Cahill, L., 2005. His brain, her brain. Scientific American 292, 40–47.

Cahill, L., 2010. Sex influences on brain and emotional memory: The burden of proof has shifted. Progress in Brain Research 186, 29–40.

Camarata, S., Woodcock, R.W., 2006. Sex differences in processing speed: Developmental effects in males and females. Intelligence 34, 231–252.

Card, N.A., Stucky, B.D., Sawalani, G.M., Little, T.D., 2008. Direct and indirect aggression during childhood and adolescence: A meta-analytic review of gender differences, intercorrelations, and relations to maladjustment. Child Development 79, 1185–1229.

Casey, B.J., Tottenham, N., Liston, C., Durston, S., 2005. Imaging the developing brain: What have we learned about cognitive development? Trends in Cognitive Sciences 9, 104–110.

Casey, B.J., Jones, R.M., Somerville, L.H., 2011. Braking and accelerating of the adolescent brain. Journal of Research on Adolescence 21, 21–33.

Ceci, S.J., Williams, W.M., 2010. Sex differences in math-intensive fields. Current Directions in Psychological Science 19, 275–279.

Chiang, M.C., McMahon, K.L., de Zubicaray, G.I., et al., 2011. Genetics of white matter development: A DTI study of 705 twins and their siblings aged 12 to 29. NeuroImage 54, 2308–2317.

Christova, P.S., Lewis, S.M., Tagaris, G.A., Uğurbil, K., Georgopoulos, A.P., 2008. A voxel-by-voxel parametric fMRI study of motor mental rotation: Hemispheric specialization and gender differences in neural processing efficiency. Experimental Brain Research 189, 79–90.

Chudowsky, N., Chudowsky, V., 2010. State Test Score Trends Through 2007–08, Part 5: Are There Differences in Achievement Between Boys and Girls? Center on Education Policy, Washington, DC.

Ciumas, C., Hirschberg, A.L., Savic, I., 2009. High fetal testosterone and sexually dimorphic cerebral networks in females. Cerebral Cortex 19, 1167–1174.

Clark, M.M., Galef, B.G., 1998. Effects of intrauterine position on the behavior and genital morphology of litter-bearing rodents. Developmental Neuropsychology 14, 197–211.

Clements, A.M., Rimrodt, S.L., Abel, J.R., et al., 2006. Sex differences in cerebral laterality of language and visuospatial processing. Brain and Language 98, 150–158.

Clements-Stephens, A.M., Rimrodt, S.L., Cutting, L.E., 2009. Developmental sex differences in basic visuospatial processing: Differences in strategy use? Neuroscience Letters 449, 155–160.

Cohen, J., 1988. Statistical Power Analysis for the Behavioral Sciences. Academic Press, New York.

Cohen-Bendahan, C.C.C., van de Beek, C., Berenbaum, S.A., 2005. Prenatal sex hormone effects on child and adult sex-typed behavior: Methods and findings. Neuroscience and Biobehavioral Reviews 29, 353–384.

Colby, J.B., Van Horn, J.D., Sowell, E.R., 2011. Quantitative in vivo evidence for broad regional gradients in the timing of white matter maturation during adolescence. NeuroImage 54, 25–31.

Cole-Harding, S., Morstad, A.L., Wilson, J.R., 1988. Spatial ability in members of opposite-sex twin pairs (abstract). Behavior Genetics 18, 710.

Connor, J.M., Serbin, L.A., 1977. Behaviorally based masculine and feminine activity-preference scales for preschoolers: Correlates with other classroom behaviors and cognitive tests. Child Development 48, 1411–1416.

Cosgrove, K.P., Mazure, C.M., Staley, J.K., 2007. Evolving knowledge of sex differences in brain structure, function, and chemistry. Biological Psychiatry 62, 847–855.

Costa Jr., P., Terracciano, A., McCrae, R.R., 2001. Gender differences in personality traits across cultures: Robust and surprising findings. Journal of Personality and Social Psychology 81, 322–331.

Craig, M.C., Fletcher, P.C., Daly, E.M., et al., 2008. Physiological variation in estradiol and brain function: A functional magnetic resonance imaging study of verbal memory across the follicular phase of the menstrual cycle. Hormones and Behavior 53, 503–508.

Crick, N.R., 1995. Relational aggression: The role of intent attributions, feelings of distress, and provocation type. Development and Psychopathology 7, 313–322.

Crick, N.R., Zahn-Waxler, C., 2003. The development of psychopathology in females and males: Current progress and future challenges. Development and Psychopathology 15, 719–742.

Critchley, H., Daly, E., Phillips, M., et al., 2000. Explicit and implicit neural mechanisms for processing of social information from facial expressions: A functional magnetic resonance imaging study. Human Brain Mapping 9, 93–105.

Dar-Nimrod, I., Heine, S.J., 2006. Exposure to scientific theories affects women's math performance. Science 314, 435.

Davatzikos, C., Resnick, S.M., 1998. Sex differences in anatomic measures of interhemispheric connectivity: Correlations with cognition in women but not men. Cerebral Cortex 8, 635–640.

De Bellis, M.D., Keshavan, M.S., Beers, S.R., et al., 2001. Sex differences in brain maturation during childhood and adolescence. Cerebral Cortex 11, 552–557.

De Lacoste-Utamsing, C., Holloway, R.L., 1982. Sexual dimorphism in the human corpus callosum. Science 216, 1431–1432.

De Vries, G.J., 2004. Minireview: Sex differences in adult and developing brains: Compensation, compensation, compensation. Endocrinology 145, 1063–1068.

Derntl, B., Habel, U., Windischberger, C., et al., 2009. General and specific responsiveness of the amygdala during explicit emotion recognition in females and males. BMC Neuroscience 10, 91.

Dessens, A.B., Slijper, F.M.E., Drop, S.L.S., 2005. Gender dysphoria and gender change in chromosomal females with congenital adrenal hyperplasia. Archives of Sexual Behavior 34, 389–397.

Diekman, A.B., Brown, E.R., Johnston, A.M., Clark, E.K., 2010. Seeking congruity between goals and roles: A new look at why women opt out of science, technology, engineering, and mathematics careers. Psychological Science 21, 1051–1057.

Dietrich, T., Krings, T., Neulen, J., et al., 2001. Effects of blood estrogen level on cortical activation patterns during cognitive activation as measured by functional MRI. NeuroImage 13, 425–432.

Dodge, K.A., Coie, J.D., Lynam, D., 2006. Aggression and antisocial behavior in youth. In: Eisenberg, N. (Ed.), Handbook of Child Psychology 6th edn. Social, Emotional, and Personality Development, vol. 3. Wiley, Hoboken, NJ.

Donnelly, K.M., Allendorfer, J.B., Szaflarski, J.P., 2011. Right hemispheric participation in semantic decision improves performance. Brain Research 1419, 105–116.

Dorfberger, S., Adi-Japhab, E., Karnia, A., 2009. Sex differences in motor performance and motor learning in children and adolescents: An increasing male advantage in motor learning and consolidation phase gains. Behavioural Brain Research 198, 165–171.

Dorn, L.D., Biro, F.M., 2011. Puberty and its measurement: A decade in review. Journal of Research on Adolescence 21, 180–195.

Dorn, L.D., Dahl, R.E., Woodward, H.R., Biro, F., 2006. Defining the boundaries of early adolescence: A user's guide to assessing pubertal status and pubertal timing in research with adolescents. Applied Developmental Science 10, 30–56.

Dubb, A., Gur, R., Avants, B., Gee, J., 2003. Characterization of sexual dimorphism in the human corpus callosum. NeuroImage 20, 512–519.

Dumas, J.A., Kutz, A.M., Naylor, M.R., Johnson, J.V., Newhouse, P.A., 2010. Increased memory load-related frontal activation after estradiol treatment in postmenopausal women. Hormones and Behavior 58, 929–935.

Eagly, A.H., Wood, W., 1999. The origins of sex differences in human behavior: Evolved dispositions versus social roles. American Psychologist 54, 408–423.

Eaton, W.O., Enns, L.R., 1986. Sex differences in human motor activity level. Psychological Bulletin 100, 19–28.

Eccles, J.S., Freedman-Doan, C., Frome, P., Jacobs, J., Yoon, K.S., 2000. Gender-role socialization in the family: A longitudinal approach. In: Eckes, T., Trautner, H.M. (Eds.), The Developmental Social Psychology of Gender. Erlbaum, Mahwah, NJ.

Eisenberg, N., Spinrad, T.L., Sadovsky, A., 2006. Empathy-related responding in children. In: Killen, M., Smetana, J.G. (Eds.), Handbook of Moral Development. Lawrence Erlbaum Associates, Mahwah, NJ.

Else-Quest, N.M., Hyde, J.S., Goldsmith, H.H., Van Hulle, C.A., 2006. Gender differences in temperament: A meta-analysis. Psychological Bulletin 132, 33–72.

Else-Quest, N.M., Hyde, J.S., Linn, M.C., 2010. Cross-national patterns of gender differences in mathematics: A meta-analysis. Psychological Bulletin 136, 103–127.

Eluvathingal, T.J., Hasan, K.M., Kramer, L., Fletcher, J.M., Ewing-Cobbs, L., 2007. Quantitative diffusion tensor tractography of association and projection fibers in normally developing children and adolescents. Cerebral Cortex 17, 2760–2768.

Erickson, K.I., Voss, M.W., Prakash, R.S., Chaddock, L., Kramer, A.F., 2010. A cross-sectional study of hormone treatment and hippocampal volume in postmenopausal women: Evidence for a limited window of opportunity. Neuropsychology 24, 68–76.

Ernst, M., Maheu, F.S., Schroth, E., et al., 2007. Amygdala function in adolescents with congenital adrenal hyperplasia: A model for the study of early steroid abnormalities. Neuropsychologia 45, 2104–2113.

Fair, D.A., Dosenbach, N.U.F., Church, J.A., et al., 2007. Development of distinct control networks through segregation and integration. Proceedings of the National Academy of Sciences of the United States of America 104, 13507–13512.

Fair, D.A., Cohen, A.L., Power, J.D., et al., 2009. Functional brain networks develop from a 'local to distributed' organization. PLoS Computational Biology 5, e1000381.

Falk, D., Froese, N., Sade, D.S., Dudek, B.G., 1999. Sex differences in brain/body relationships of rhesus monkeys and humans. Journal of Human Evolution 36, 233–238.

Feng, J., Spence, I., Pratt, J., 2007. Playing an action video game reduces gender differences in spatial cognition. Psychological Science 18, 850–855.

Fernández, G., Weis, S., Stoffel-Wagner, B., et al., 2003. Menstrual cycle-dependent neural plasticity in the adult human brain is hormone, task, and region specific. Journal of Neuroscience 23, 3790–3795.

Fiedler, K., 2011. Voodoo correlations are everywhere-not only in neuroscience. Perspectives on Psychological Science 6, 163–171.

Filipek, P.A., Richelme, C., Kennedy, D.N., Caviness, V.S., 1994. The young adult human brain: An MRI-based morphometric analysis. Cerebral Cortex 4, 344–360.

Fine, C., 2010. Delusions of Gender: How Our Minds, Society, and Neurosexism Create Difference. W.W. Norton, New York.

Fivush, R., 1998. Gendered narratives: Elaboration, structure, and emotion in parent-child reminiscing across the preschool years. In: Thompson, C.P., Herrmann, D.J. (Eds.), Autobiographical Memory: Theoretical and Applied Perspectives. Lawrence Erlbaum Associates, Mahwah, NJ.

Fivush, R., Buckner, J.P., 2000. Gender, sadness, and depression: The development of emotional focus through gendered discourse. In: Fischer, A.H. (Ed.), Gender and Emotion: Social Psychological Perspectives. Studies in Emotion and Social InteractionCambridge University Press, New York.

Flashman, L.A., Andreasen, N.C., Flaum, M., Swayze, V.W., 1997. Intelligence and regional brain volumes in normal controls. Intelligence 25, 149–160.

Forbes, E.E., Dahl, R.E., 2010. Pubertal development and behavior: Hormonal activation of social and motivational tendencies. Brain and Cognition 72, 66–72.

Forbes, E.E., Ryan, N.D., Phillips, M.L., et al., 2010. Healthy adolescents' neural response to reward: Associations with puberty, positive affect, and depressive symptoms. Journal of the American Academy of Child and Adolescent Psychiatry 49, 162–172.

Friston, K.J., 2004. Human Brain Function. Elsevier, San Diego, CA.

Frost, J.A., Binder, J.R., Springer, J.A., et al., 1999. Language processing is strongly left lateralized in both sexes: Evidence from functional MRI. Brain 122, 199–208.

Fusar-Poli, P., Placentino, A., Carletti, F., et al., 2009. Functional atlas of emotional faces processing: A voxel-based meta-analysis of 105 functional magnetic resonance imaging studies. Journal of Psychiatry & Neuroscience 34, 418–432.

Gates, K.M., Molenaar, P.C.M., Hillary, F.G., Ram, N., Rovine, M.J., 2010. Automatic search for fMRI connectivity mapping: An alternative to granger causality testing using formal equivalences among SEM path modeling, VAR, and unified SEM. NeuroImage 50, 1118–1125.

Gates, K.M., Molenaar, P.C.M., Hillary, F.G., Slobounov, S., 2011. Extended unified SEM approach for modeling event-related fMRI data. NeuroImage 54, 1151–1158.

Gauthier, C.T., Duyme, M., Zanca, M., Capron, C., 2009. Sex and performance level effects on brain activation during a verbal fluency task: A functional magnetic resonance imaging study. Cortex 45, 164–176.

Geary, D.C., 1998. Male, Female: The Evolution of Human Sex Differences. American Psychological Association, Washington, DC.

Geiser, C., Lehmann, W., Eid, M., 2008. A note on sex differences in mental rotation in different age groups. Intelligence 36, 556–563.

Gentile, B., Grabe, S., Dolan-Pascoe, B., Twenge, J.M., Wells, B.E., Maitino, A., 2009. Gender differences in domain-specific self-esteem: A meta-analysis. Review of General Psychology 13, 34–45.

Gibber, J., Goy, R.W., 1985. Infant directed behavior in young rhesus monkey: Sex difference and effects of prenatal androgen. American Journal of Primatology 8, 235–237.

Giedd, J.N., Castellanos, F.X., Rajapakse, J.C., Vaituzis, A.C., Rapoport, J.L., 1997. Sexual dimorphism of the developing human brain. Progress in Neuro-Psychopharmacology & Biological Psychiatry 21, 1185–1201.

Giedd, J.N., Blumenthal, J., Jeffries, N.O., et al., 1999. Brain development during childhood and adolescence: A longitudinal MRI study. Nature Neuroscience 2, 861–863.

Giedd, J.N., Clasen, L.S., Lenroot, R., et al., 2006. Puberty-related influences on brain development. Molecular and Cellular Endocrinology 254, 154–162.

Giedd, J.N., Rapoport, J.L., 2010. Structural MRI of pediatric brain development: What have we learned and where are we going? Neuron 67, 728–734.

Giorgio, A., Watkins, K.E., Douaud, G., et al., 2008. Changes in white matter microstructure during adolescence. NeuroImage 39, 52–61.

Gogtay, N., Giedd, J.N., Lusk, L., et al., 2004. Dynamic mapping of human cortical development during childhood through early adulthood. Proceedings of the National Academy of Sciences of the United States of America 101, 8174–8179.

Goldstein, J.M., Seidman, L.J., Horton, N.J., et al., 2001. Normal sexual dimorphism of the adult human brain assessed by in vivo magnetic resonance imaging. Cerebral Cortex 11, 490–497.

Gorski, R.A., Gordon, J.H., Shryne, J.E., Southam, A.M., 1978. Evidence for a morphological sex difference within the medial preoptic area of the rat brain. Brain Research 148, 333–346.

Goto, M., Abe, O., Miyati, T., et al., 2011. 3 tesla MRI detects accelerated hippocampal volume reduction in postmenopausal women. Journal of Magnetic Resonance Imaging 33, 48–53.

Goy, R.W., McEwen, B.S., 1980. Sexual Differentiation of the Brain. MIT Press, Cambridge.

Goy, R.W., Bercovitch, F.B., McBrair, M.C., 1988. Behavioral masculinization is independent of genital masculinization in prenatally androgenized female rhesus macaques. Hormones and Behavior 22, 552–571.

Grimshaw, G.M., Bryden, M.P., Finegan, J.A.K., 1995a. Relations between prenatal testosterone and cerebral lateralization in children. Neuropsychology 9, 68–79.

Grimshaw, G.M., Sitarenios, G., Finegan, J.A., 1995b. Mental rotation at 7 years: Relations with prenatal testosterone levels and spatial play experience. Brain and Cognition 29, 85–100.

Grön, G., Wunderlich, A.P., Spitzer, M., Tomczak, R., Riepe, M.W., 2000. Brain activation during human navigation: Gender-different neural networks as substrate of performance. Nature Neuroscience 3, 404–408.

Guiso, L., Monte, F., Sapienza, P., Zingales, L., 2008. Culture, gender, and math. Science 320, 1164–1165.

Gur, R.C., Turetsky, B.I., Matsui, M., et al., 1999. Sex differences in brain gray and white matter in healthy young adults: Correlations with cognitive performance. Journal of Neuroscience 19, 4065–4072.

Gur, R.C., Alsop, D., Glahn, D., et al., 2000. An fMRI study of sex differences in regional activation to a verbal and a spatial task. Brain and Language 74, 157–170.

Habel, U., Windischberger, C., Derntl, B., et al., 2007. Amygdala activation and facial expressions: Explicit emotion discrimination versus implicit emotion processing. Neuropsychologia 45, 2369–2377.

Halari, R., Sharma, T., Hines, M., Andrew, C., Simmons, A., Kumari, V., 2006. Comparable fMRI activity with differential behavioural performance on mental rotation and overt verbal fluency tasks in healthy men and women. Experimental Brain Research 169, 1–14.

Hall, J.J., Neal, T.J., Dean, R.S., 2008. Lateralization of cerebral functions. In: Horton, A.M., Wedding, D. (Eds.), The Neuropsychology Handbook. 3rd edn. Springer, New York.

Halpern, D.F., 1986. A different answer to the question, 'do sex-related differences in spatial abilities exist?'. American Psychologist 41, 1014–1015.

Halpern, D.F., 2012. Sex Differences in Cognitive Abilities. Psychology Press, New York.

Halpern, D.F., Benbow, C.P., Geary, D.C., Gur, R.C., Hyde, J.S., Gernsbacher, M.A., 2007. The science of sex differences in science and mathematics. Psychological Science in the Public Interest 8, 1–51.

Hamann, S., 2005. Sex differences in the responses of the human amygdala. The Neuroscientist 11, 288–293.

Hampson, E., 2007. Endocrine contributions to sex differences in visuospatial perception and cognition. In: Becker, J.B., Berkley, K.J., Geary, N., Hampson, E., Herman, J., Young, E. (Eds.), Sex Differences in the Brain: From Genes to Behavior. Oxford University Press, New York.

Hampson, E., Rovet, J.F., Altmann, D., 1998. Spatial reasoning in children with congenital adrenal hyperplasia due to 21-hydroxylase deficiency. Developmental Neuropsychology 14, 299–320.

Hannagan, R.J., 2008. Gendered political behavior: A Darwinian feminist approach. Sex Roles 59, 465–475.

Harasty, J., Double, K.L., Halliday, G.M., Kril, J.J., McRitchie, D.A., 1997. Language-associated cortical regions are proportionally larger in the female brain. Archives of Neurology 54, 171–176.

Hariri, A.R., Bookheimer, S.Y., Mazziotta, J.C., 2000. Modulating emotional responses: Effects of a neocortical network on the limbic system. NeuroReport 11, 43–48.

Hartung, C.M., Widiger, T.A., 1998. Gender differences in the diagnosis of mental disorders: Conclusions and controversies of the DSM-IV. Psychological Bulletin 123, 260–278.

Hedges, L.V., Nowell, A., 1995. Sex differences in mental test scores, variability, and numbers of high-scoring individuals. Science 269, 41–45.

Heil, M., Kavsek, M., Rolke, B., Beste, C., Jansen, P., 2011. Mental rotation in female fraternal twins: Evidence for intra-uterine hormone transfer? Biological Psychology 86, 90–93.

Herlitz, A., Lovén, J., Thilers, P., Rehnman, J., 2010. Sex differences in episodic memory: The where but not the why. In: Bäckman, L., Nyberg, L. (Eds.), Memory, Aging and the Brain. Psychology Press, New York.

Herting, M.M., Maxwell, E.C., Irvine, C., Nagel, B.J., 2012. The impact of sex, puberty, and hormones on white matter microstructure in adolescents. Cerebral Cortex 22, 1979–1992.

Hier, D.B., Crowley, W.F., 1982. Spatial ability in androgen-deficient men. The New England Journal of Medicine 302, 1202–1205.

Hines, M., 2010. Sex-related variation in human behavior and the brain. Trends in Cognitive Sciences 14, 448–456.

Hines, M., 2011. Gender development and the human brain. Annual Review of Neuroscience 34, 69–88.

Hines, M., McAdams, L.A., Chiu, L., Bentler, P.M., Lipcamon, J., 1992. Cognition and the corpus callosum: Verbal fluency, visuospatial ability, and language lateralization related to midsaggital surface areas of callosal subregions. Behavioral Neuroscience 106, 3–14.

Hines, M., Ahmed, F., Hughes, I.A., 2003a. Psychological outcomes and gender-related development in complete androgen insensitivity syndrome. Archives of Sexual Behavior 32, 93–101.

Hines, M., Fane, B.A., Pasterski, V.L., Mathews, G.A., Conway, G.S., Brook, C., 2003b. Spatial abilities following prenatal androgen abnormality: Targeting and mental rotations performance in

individuals with congenital adrenal hyperplasia. Psychoneuroendocrinology 28, 1010–1026.

Holloway, R.L., 1980. Within-species brain-body weight variability: A reexamination of the Danish data and other primate species. American Journal of Physical Anthropology 53, 109–121.

Hugdahl, K., Thomsen, T., Ersland, L., 2006. Sex differences in visuospatial processing: An fMRI study of mental rotation. Neuropsychologia 44, 1575–1583.

Hulshoff Pol, H.E., Cohen-Kettenis, P.T., Van Haren, N.E.M., et al., 2006. Changing your sex changes your brain: Influences of testosterone and estrogen on adult human brain structure. European Journal of Endocrinology 155, S107–S114.

Hyde, J.S., 2005. The gender similarities hypothesis. American Psychologist 60, 581–592.

Im, K., Lee, J.M., Lee, J., et al., 2006. Gender difference analysis of cortical thickness in healthy young adults with surface-based methods. NeuroImage 31, 31–38.

Im, K., Lee, J.M., Lyttelton, O., Kim, S.H., Evans, A.C., Kim, S.I., 2008. Brain size and cortical structure in the adult human brain. Cerebral Cortex 18, 2181–2191.

Johnson, W., Bouchard, T.J., 2007. Sex differences in mental abilities: G masks the dimensions on which they lie. Intelligence 35, 23–39.

Jordan, K., Wurstenberg, T., Heinze, H.J., Peters, M., Jancke, L., 2002. Women and men exhibit different cortical activation patterns during mental rotation tasks. Neuropsychologia 40, 2397–2408.

Jordan-Young, R.M., 2010. Brain Storm: The Flaws in the Science of Sex Differences. Harvard University Press, Cambridge, MA.

Kansaku, K., Kitazawa, S., 2001. Imaging studies on sex differences in the lateralization of language. Neuroscience Research 41, 333–337.

Kim, J., Zhu, W., Chang, L., Bentler, P.M., Ernst, T., 2007. Unified structural equation modeling approach for the analysis of multisubject, multivariate functional MRI data. Human Brain Mapping 28, 85–93.

Kimura, D., 1999. Sex and Cognition. MIT Press, Cambridge, MA.

Kitazawa, S., Kansaku, K., 2005. Sex difference in language lateralization may be task-dependent. Brain 128, E30.

Kling, K.C., Hyde, J.S., Showers, C.J., Buswell, B.N., 1999. Gender differences in self-esteem: A meta-analysis. Psychological Bulletin 125, 470–500.

Knickmeyer, R.C., Davenport, M., 2011. Turner syndrome and sexual differentiation of the brain: Implications for understanding male-biased neurodevelopmental disorders. Journal of Neurodevelopmental Disorders 3, 293–306.

Konrad, C., Engelien, A., Schöning, S., et al., 2008. The functional anatomy of semantic retrieval is influenced by gender, menstrual cycle, and sex hormones. Journal of Neural Transmission 115, 1327–1337.

Koscik, T., O'Leary, D., Moser, D.J., Andreasen, N.C., Nopoulos, P., 2009. Sex differences in parietal lobe morphology: Relationship to mental rotation performance. Brain and Cognition 69, 451–459.

Kyratzis, A., 2001. Emotion talk in preschool same-sex friendship groups: Fluidity over time and context. Early Education and Development 12, 359–392.

Lansdell, H., Davie, J.C., 1972. Massa intermedia: Possible relation to intelligence. Neuropsychologia 10, 207–210.

Largo, R.H., Caflisch, J.A., Hug, F., Muggli, K., Molnar, A.A., Molinari, L., 2001a. Neuromotor development from 5 to 18 years. Part 2: Associated movements. Developmental Medicine and Child Neurology 43, 444–453.

Largo, R.H., Caflisch, J.A., Hug, F., et al., 2001b. Neuromotor development from 5 to 18 years. Part 1: Timed performance. Developmental Medicine and Child Neurology 43, 436–443.

Lawton, C.A., 2010. Gender, spatial abilities, and wayfinding. In: Chrisler, J.C., McCreary, D.R. (Eds.), Handbook of Gender Research in Psychology. Gender Research in General and Experimental Psychology, vol. 1. Springer Science + Business Media, New York.

Lebel, C., Walker, L., Leemans, A., Phillips, L., Beaulieu, C., 2008. Microstructural maturation of the human brain from childhood to adulthood. NeuroImage 40, 1044–1055.

Lenroot, R.K., Giedd, J.N., 2010. Sex differences in the adolescent brain. Brain and Cognition 72, 46–55.

Lenroot, R.K., Gogtay, N., Greenstein, D.K., et al., 2007. Sexual dimorphism of brain developmental trajectories during childhood and adolescence. NeuroImage 36, 1065–1073.

Lentini, E., Kasahara, M., Arver, S., Savic, I., 2012. Sex differences in the human brain and the impact of sex chromosomes and sex hormones. Cerebral Cortex.

Leonard, C.M., Towler, S., Welcome, S., et al., 2008. Size matters: Cerebral volume influences sex differences in neuroanatomy. Cerebral Cortex 18, 2920–2931.

Lepage, J.F., Mazaika, P.K., Hong, D.S., Raman, M., Reiss, A.L., 2012. Cortical brain morphology in young, estrogen-naive, and adolescent, estrogen-treated girls with Turner Syndrome. Cerebral Cortex.

LeVay, S., 1991. A difference in hypothalamic structure between heterosexual and homosexual men. Science 253, 1034–1037.

Levine, S.C., Vasilyeva, M., Lourenco, S.F., Newcombe, N.S., Huttenlocher, J., 2005. Socioeconomic status modifies the sex difference in spatial skill. Psychological Science 16, 841–845.

Liben, L.S., 1995. Psychology meets geography: Exploring the gender gap on the national geography bee. Psychological Science Agenda 8, 8–9.

Lindberg, S.M., Hyde, J.S., Petersen, J.L., Linn, M.C., 2010. New trends in gender and mathematics performance: A meta-analysis. Psychological Bulletin 136, 1123–1135.

Lombardo, M.V., Ashwin, E., Auyeung, B., et al., 2012. Fetal testosterone influences sexually dimorphic gray matter in the human brain. Journal of Neuroscience 32, 674–680.

Lord, C., Buss, C., Lupien, S.J., Pruessner, J.C., 2008. Hippocampal volumes are larger in postmenopausal women using estrogen therapy compared to past users, never users and men: A possible window of opportunity effect. Neurobiology of Aging 29, 95–101.

Luders, E., Steinmetz, H., Jancke, L., 2002. Brain size and grey matter volume in the healthy human brain. NeuroReport 13, 2371–2374.

Luders, E., Narr, K.I., Thompson, P.M., et al., 2004. Gender differences in cortical complexity. Nature Neuroscience 7, 799–800.

Luders, E., Harr, K.L., Thompson, P.M., et al., 2006a. Gender effects on cortical thickness and the influence of scaling. Human Brain Mapping 27, 314–324.

Luders, E., Narr, K.L., Zaidel, E., Thompson, P.M., Toga, A.W., 2006b. Gender effects on callosal thickness in scaled and unscaled space. NeuroReport 17, 1103–1106.

Luders, E., Thompson, P.M., Narr, K.L., Toga, A.W., Jancke, L., Gaser, C., 2006c. A curvature-based approach to estimate local gyrification on the cortical surface. NeuroImage 29, 1224–1230.

Luders, E., Gaser, C., Narr, K.L., Toga, A.W., 2009a. Why sex matters: Brain size independent differences in gray matter distributions between men and women. Journal of Neuroscience 29, 14265–14270.

Luders, E., Narr, K.L., Thompson, P.M., Toga, A.W., 2009b. Neuroanatomical correlates of intelligence. Intelligence 37, 156–163.

Luders, E., Thompson, P.M., Toga, A.W., 2010. The development of the corpus callosum in the healthy human brain. Journal of Neuroscience 30, 10985–10990.

Luders, E., Toga, A.W., 2010. Sex differences in brain anatomy. Progress in Brain Research 186, 3–12.

Luders, E., Thompson, P.M., Narr, K.L., et al., 2011. The link between callosal thickness and intelligence in healthy children and adolescents. NeuroImage 54, 1823–1830.

Luna, B., Velanova, K., Geier, C.F., 2010. Methodological approaches in developmental neuroimaging studies. Human Brain Mapping 31, 863–871.

Lust, J.M., Geuze, R.H., Van de Beek, C., Cohen-Kettenis, P.T., Groothuis, A.G.G., Bouma, A., 2010. Sex specific effect of prenatal testosterone on language lateralization in children. Neuropsychologia 48, 536–540.

Lv, B., Li, J., He, H.G., et al., 2010. Gender consistency and difference in healthy adults revealed by cortical thickness. NeuroImage 53, 373–382.

Maccoby, E.E., 1998. The Two Sexes: Growing Up Apart, Coming Together. Harvard University Press, Cambridge, MA.

Maguire, E.A., Gadian, D.G., Johnsrude, I.S., et al., 2000. Navigation-related structural change in the hippocampi of taxi drivers. Proceedings of the National Academy of Sciences of the United States of America 97, 4398–4403.

Maguire, E.A., Spiers, H.J., Good, C.D., Hartley, T., Frackowiak, R.S.J., Burgess, N., 2003. Navigation expertise and the human hippocampus: A structural brain imaging analysis. Hippocampus 13, 250–259.

Maki, P.M., 2005. Estrogen effects on the hippocampus and frontal lobes. International Journal of Fertility and Women's Medicine 50, 67–71.

Maki, P.M., Resnick, S.M., 2000. Longitudinal effects of estrogen replacement therapy on PET cerebral blood flow and cognition. Neurobiology of Aging 21, 373–383.

Maki, P.M., Resnick, S.M., 2001. Effects of estrogen on patterns of brain activity at rest and during cognitive activity: A review of neuroimaging studies. NeuroImage 14, 789–801.

Maki, P.M., Sundermann, E., 2009. Hormone therapy and cognitive function. Human Reproduction Update 15, 667–681.

Malouf, M.A., Migeon, C.J., Carson, K.A., Petrucci, L., Wisniewski, A.B., 2006. Cognitive outcome in adult women affected by congenital adrenal hyperplasia due to 21-hydroxylase deficiency. Hormone Research 65, 142–150.

Martel, M.M., Klump, K., Nigg, J.T., Breedlove, S.M., Sisk, C.L., 2009. Potential hormonal mechanisms of attention-deficit/hyperactivity disorder and major depressive disorder: A new perspective. Hormones and Behavior 55, 465–479.

Martin, C.L., Fabes, R.A., 2001. The stability and consequences of young children's same-sex peer interactions. Developmental Psychology 37, 431–446.

Martin, C.L., Ruble, D.N., 2010. Patterns of gender development. Annual Review of Psychology 61, 353–381.

Martin, C.L., Ruble, D.N., Szkrybalo, J., 2002. Cognitive theories of early gender development. Psychological Bulletin 128, 903–933.

Mazzone, L., Mueller, S.C., Maheu, F., VanRyzin, C., Merke, D.P., Ernst, M., 2011. Emotional memory in early steroid abnormalities: An fMRI study of adolescents with congenital adrenal hyperplasia. Developmental Neuropsychology 36, 473–492.

McCabe, D.P., Castel, A.D., 2008. Seeing is believing: The effect of brain images on judgments of scientific reasoning. Cognition 107, 343–352.

McCarthy, M.M., Arnold, A.P., 2011. Reframing sexual differentiation of the brain. Nature Neuroscience 14, 677–683.

McClure, E.B., 2000. A meta-analytic review of sex differences in facial expression processing and their development in infants, children, and adolescents. Psychological Bulletin 126, 424–453.

McClure, E.B., Monk, C.S., Nelson, E.E., et al., 2004. A developmental examination of gender differences in brain engagement during evaluation of threat. Biological Psychiatry 55, 1047–1055.

McGlone, J., 1980. Sex differences in human brain asymmetry: A critical survey. The Behavioral and Brain Sciences 3, 215–227.

Merke, D.P., Fields, J.D., Keil, M.F., Vaituzis, A.C., Chrousos, G.P., Giedd, J.N., 2003. Children with classic congenital adrenal hyperplasia have decreased amygdala volume: Potential prenatal and postnatal hormonal effects. Journal of Clinical Endocrinology and Metabolism 88, 1760–1765.

Meyer, G.J., Finn, S.E., Eyde, L.D., et al., 2001. Psychological testing and psychological assessment: A review of evidence and issues. American Psychologist 56, 128–165.

Meyer-Bahlburg, H.F.L., 2005. Gender identity outcome in female-raised 46, XY persons with penile agenesis, cloacal exstrophy of the bladder, or penile ablation. Archives of Sexual Behavior 34, 423–438.

Meyer-Bahlburg, H.F.L., Dolezal, C., Baker, S.W., Ehrhardt, A.A., New, M.I., 2006. Gender development in women with congenital adrenal hyperplasia as a function of disorder severity. Archives of Sexual Behavior 35, 667–684.

Moffitt, T.E., Caspi, A., Rutter, M., Silva, P.A., 2001. Sex Differences in Antisocial Behaviour: Conduct Disorder, Delinquency, and Violence in the Dunedin Longitudinal Study. Cambridge University Press, New York.

Mondschein, E.R., Adolph, K.E., Tamis-LeMonda, C.S., 2000. Gender bias in mothers' expectations about infant crawling. Journal of Experimental Child Psychology 77, 304–316.

Money, J., Ehrhardt, A.A., 1972. Man and Woman, Boy and Girl. Johns Hopkins University Press, Baltimore, MD.

Moore, D.S., Johnson, S.P., 2008. Mental rotation in human infants: A sex difference. Psychological Science 19, 1063–1066.

Morrongiello, B.A., Matheis, S., 2007. Understanding children's injury-risk behaviors: The independent contributions of cognitions and emotions. Journal of Pediatric Psychology 32, 926–937.

Mueller, S.C., Temple, V., Oh, E., et al., 2008. Early androgen exposure modulates spatial cognition in congenital adrenal hyperplasia (CAH). Psychoneuroendocrinology 33, 973–980.

Mueller, S.C., Mandell, D., Leschek, E.W., Pine, D.S., Merke, D.P., Ernst, M., 2009. Early hyperandrogenism affects the development of hippocampal function: Preliminary evidence from a functional magnetic resonance imaging study of boys with familial male precocious puberty. Journal of Child and Adolescent Psychopharmacology 19, 41–50.

Mueller, S.C., Merke, D.P., Leschek, E.W., et al., 2011a. Grey matter volume correlates with virtual water maze task performance in boys with androgen excess. Neuroscience 197, 225–232.

Mueller, S.C., Merke, D.P., Leschek, E.W., Fromm, S., VanRyzin, C., Ernst, M., 2011b. Increased medial temporal lobe and striatal grey-matter volume in a rare disorder of androgen excess: A voxel-based morphometry (VBM) study. The International Journal of Neuropsychopharmacology 14, 445–457.

Nelson, C., Righi, G., 2013. Face processing. Neural Circuit Development and Function in the Healthy and Diseased Brain: Comprehensive Developmental Neuroscience, Volume 3. Elsevier, Oxford.

Newcombe, N., Dubas, J.S., 1992. A longitudinal study of predictors of spatial ability in adolescent females. Child Development 63, 37–46.

Newcombe, N., Bandura, M.M., Taylor, D.G., 1983. Sex differences in spatial ability and spatial activities. Sex Roles 9, 377–386.

Nolen-Hoeksema, S., Hilt, L., 2009. Gender differences in depression. In: Gotlieb, I.H., Hammen, C.L. (Eds.), Handbook of Depression. 2nd edn. Guilford, New York.

Nopoulos, P., Flaum, M., O'Leary, D., Andreasen, N.C., 2000. Sexual dimorphism in the human brain: Evaluation of tissue volume, tissue composition and surface anatomy using magnetic resonance imaging. Psychiatry Research: Neuroimaging 98, 1–13.

Nordenström, A., Servin, A., Bohlin, G., Larsson, A., Wedell, A., 2002. Sex-typed toy play behavior correlates with the degree of prenatal androgen exposure assessed by CYP21 genotype in girls with congenital adrenal hyperplasia. Journal of Clinical Endocrinology and Metabolism 87, 5119–5124.

Ohnishi, T., Matsuda, H., Hirakata, M., Ugawa, Y., 2006. Navigation ability dependent neural activation in the human brain: An fMRI study. Neuroscience Research 55, 361–369.

Ortigue, S., Thut, G., Landis, T., Michel, C.M., 2005. Time-resolved sex differences in language lateralization. Brain 128, E28.

Pasterski, V.L., Geffner, M.E., Brain, C., Hindmarsh, P., Brook, C., Hines, M., 2005. Prenatal hormones and postnatal socialization by parents as determinants of male-typical toy play in girls with congenital adrenal hyperplasia. Child Development 76, 264–278.

Paus, T., 2010. Sex differences in the human brain: A developmental perspective. Progress in Brain Research 186, 13–28.

Paus, T., Nawaz-Khan, I., Leonard, G., et al., 2010. Sexual dimorphism in the adolescent brain: Role of testosterone and androgen receptor in global and local volumes of grey and white matter. Hormones and Behavior 57, 63–75.

Peper, J.S., Hulshoff Pol, H.E., Crone, E.A., van Honk, J., 2011. Sex steroids and brain structure in pubertal boys and girls: A mini-review of neuroimaging studies. Neuroscience 191, 28–37.

Perrin, J.S., Hervé, P.-Y., Leonard, G., et al., 2008. Growth of white matter in the adolescent brain: Role of testosterone and androgen receptor. Journal of Neuroscience 28, 9519–9524.

Persad, C.C., Zubieta, J.K., Love, T., Wang, H., Tkaczyk, A., Smith, Y.R., 2009. Enhanced neuroactivation during verbal memory processing in postmenopausal women receiving short-term hormone therapy. Fertility and Sterility 92, 197–204.

Pessoa, L., Adolphs, R., 2010. Emotion processing and the amygdala: From a 'low road' to 'many roads' of evaluating biological significance. Nature Reviews Neuroscience 11, 773–782.

Peters, M., 1991. Sex differences in human brain size and the general meaning of differences in brain size. Canadian Journal of Psychology 45, 507–522.

Peters, M., Battista, C., 2008. Applications of mental rotation figures of the shepard and metzler type and description of a mental rotation stimulus library. Brain and Cognition 66, 260–264.

Peters, M., Jäncke, L., Staiger, J.F., Schlaug, G., Huang, Y., Steinmetz, H., 1998. Unsolved problems in comparing brain sizes in homo sapiens. Brain and Cognition 37, 254–285.

Phoenix, C.H., Goy, R.W., Gerall, A.A., Young, W.C., 1959. Organizing action of prenatally administered testosterone propionate on the tissues mediating mating behavior in the female guinea pig. Endocrinology 65, 369–382.

Phoenix, C.H., Slob, A.K., Goy, R.W., 1973. Effects of castration and replacement therapy on sexual behavior of adult male rhesuses. Journal of Comparative and Physiological Psychology 84, 472–481.

Plante, E., Schmithorst, V.J., Holland, S.K., Byars, A.W., 2006. Sex differences in the activation of language cortex during childhood. Neuropsychologia 44, 1210–1221.

Poldrack, R.A., 2000. Imaging brain plasticity: Conceptual and methodological issues – A theoretical review. NeuroImage 12, 1–13.

Protopopescu, X., Butler, T., Pan, H., et al., 2008. Hippocampal structural changes across the menstrual cycle. Hippocampus 18, 985–988.

Puts, D.A., McDaniel, M.A., Jordan, C.L., Breedlove, N.J., 2008. Spatial ability and prenatal androgens: Meta-analyses of congenital adrenal hyperplasia and digit ratio (2D:4D) studies. Archives of Sexual Behavior 37, 100–111.

Puts, D.A., Cárdenas, R.A., Bailey, D.H., Burriss, R.P., Jordan, C.L., Breedlove, S.M., 2010. Salivary testosterone does not predict mental rotation performance in men or women. Hormones and Behavior 58, 282–289.

Quinn, P.C., Liben, L.S., 2008. A sex difference in mental rotation in young infants. Psychological Science 19, 1067–1070.

Rabinowicz, T., Dean, D.E., Petetot, J.M.C., de Courten-Myers, G.M., 1999. Gender differences in the human cerebral cortex: More neurons in males; more processes in females. Journal of Child Neurology 14, 98–107.

Rabl, R., 1958. Strukturstudien an der aassa intermedia des thalamus opticus. Journal für Hirnforschung 4, 78–112.

Raznahan, A., Lee, Y., Stidd, R., et al., 2010. Longitudinally mapping the influence of sex and androgen signaling on the dynamics of human cortical maturation in adolescence. Proceedings of the National Academy of Sciences of the United States of America 107, 16988–16993.

Reinius, B., Jazin, E., 2009. Prenatal sex differences in the human brain. Molecular Psychiatry 14, 988–989.

Resnick, S.M., Berenbaum, S.A., Gottesman, I.I., Bouchard, T.J., 1986. Early hormonal influences on cognitive functioning in congenital adrenal hyperplasia. Developmental Psychology 22, 191–198.

Resnick, S.M., Maki, P.M., Golski, S., Kraut, M.A., Zonderman, A.B., 1998. Effects of estrogen replacement therapy on pet cerebral blood flow and neuropsychological performance. Hormones and Behavior 34, 171–182.

Resnick, S.M., Espeland, M.A., Jaramillo, S.A., et al., 2009. Postmenopausal hormone therapy and regional brain volumes the WHIMS-MRI study. Neurology 72, 135–142.

Robertson, D., Craig, M., van Amelsvoort, T., et al., 2009. Effects of estrogen therapy on age-related differences in gray matter concentration. Climacteric 12, 301–309.

Roivainen, E., 2011. Gender differences in processing speed: A review of recent research. Learning and Individual Differences 21, 145–149.

Ross, J., Roeltgen, D., Zinn, A., 2006. Cognition and the sex chromosomes: Studies in Turner syndrome. Hormone Research 65, 47–56.

Rubenstein, J.L.R., Rakic, P., 2013. Patterning and Cell Types Specification in the Developing CNS and PNS.

Rubia, K., Hyde, Z., Halari, R., Giampietro, V., Smith, A., 2010. Effects of age and sex on developmental neural networks of visual-spatial attention allocation. NeuroImage 51, 817–827.

Ruble, D.N., Martin, C.L., Berenbaum, S.A., 2006. Gender development. In: Eisenberg, N. (Ed.), Handbook of Child Psychology. 6th ed Social, Emotional, and Personality Development, vol. 3. Wiley, Hoboken, NJ.

Rutter, M., Giller, H., Hagell, A., 1998. Antisocial Behavior by Young People. Cambridge University Press, New York.

Ryan, B.C., Vandenbergh, J.G., 2002. Intrauterine position effects. Neuroscience and Biobehavioral Reviews 26, 665–678.

Savic, I., Garcia-Falgueras, A., Swaab, D.F., 2010. Sexual differentiation of the human brain in relation to gender identity and sexual orientation. Progress in Brain Research 186, 41–62.

Schmithorst, V.J., Yuan, W.H., 2010. White matter development during adolescence as shown by diffusion MRI. Brain and Cognition 72, 16–25.

Schneider, S., Peters, J., Bromberg, U., et al., 2011. Boys do it the right way: Sex-dependent amygdala lateralization during face processing in adolescents. NeuroImage 56, 1847–1853.

Schöning, S., Engelien, A., Kugel, H., et al., 2007. Functional anatomy of visuo-spatial working memory during mental rotation is influenced by sex, menstrual cycle, and sex steroid hormones. Neuropsychologia 45, 3203–3214.

Schulz, K.M., Zehr, J.L., Salas-Ramirez, K.Y., Sisk, C.L., 2009. Testosterone programs adult social behavior before and during, but not after, adolescence. Endocrinology 150, 3690–3698.

Seldon, H.L., 2005. Does brain white matter growth expand the cortex like a balloon? Hypothesis and consequences. Laterality 10, 81–95.

Sergerie, K., Chochol, C., Armony, J.L., 2008. The role of the amygdala in emotional processing: A quantitative meta-analysis of functional neuroimaging studies. Neuroscience and Biobehavioral Reviews 32, 811–830.

Shaw, P., Greenstein, D., Lerch, J., et al., 2006. Intellectual ability and cortical development in children and adolescents. Nature 440, 676–679.

Shaw, P., Gogtay, N., Rapoport, J., 2010. Childhood psychiatric disorders as anomalies in neurodevelopmental trajectories. Human Brain Mapping 31, 917–925.

II. COGNITIVE DEVELOPMENT

Shaywitz, B.A., Shaywitz, S.E., Pugh, K.R., et al., 1995. Sex differences in the functional organization of the brain for language. Nature 373, 607–609.

Shaywitz, S.E., Shaywitz, B.A., Pugh, K.R., et al., 1999. Effect of estrogen on brain activation patterns in postmenopausal women during working memory tasks. Journal of the American Medical Association 281, 1197–1202.

Simpkins, S.D., Davis-Kean, P.E., Eccles, J.S., 2005. Parents' socializing behavior and children's participation in math, science, and computer out-of-school activities. Applied Developmental Science 9, 14–30.

Sisk, C.L., Zehr, J.L., 2005. Pubertal hormones organize the adolescent brain and behavior. Frontiers in Neuroendocrinology 26, 163–174.

Sneider, J.T., Sava, S., Rogowska, J., Yurgelun-Todd, D.A., 2011. A preliminary study of sex differences in brain activation during a spatial navigation task in healthy adults. Perceptual and Motor Skills 113, 461–480.

Sommer, I.E.C., Aleman, A., Bouma, A., Kahn, R.S., 2004. Do women really have more bilateral language representation than men? A meta-analysis of functional imaging studies. Brain 127, 1845–1852.

Sommer, I.E., Aleman, A., Somers, M., Boks, M.P., Kahn, R.S., 2008. Sex differences in handedness, asymmetry of the planum temporale and functional language lateralization. Brain Research 1206, 76–88.

Song, M., Zhou, Y., Li, J., et al., 2008. Brain spontaneous functional connectivity and intelligence. NeuroImage 41, 1168–1176.

Sowell, E.R., Thompson, P.M., Tessner, K.D., Toga, A.W., 2001. Mapping continued brain growth and gray matter density reduction in dorsal frontal cortex: Inverse relationships during postadolescent brain maturation. Journal of Neuroscience 21, 8819–8829.

Sowell, E.R., Trauner, D.A., Gamst, A., Jernigan, T.L., 2002. Development of cortical and subcortical brain structures in childhood and adolescence: A structural MRI study. Developmental Medicine and Child Neurology 44, 4–16.

Sowell, E.R., Peterson, B.S., Kan, E., et al., 2007. Sex differences in cortical thickness mapped in 176 healthy individuals between 7 and 87 years of age. Cerebral Cortex 17, 1550–1560.

Sowell, E., Colby, J., O'Hare, E.D., 2013. Brain development: Birth through adolescence. Neural Circuit Development and Function in the Healthy and Diseased Brain: Comprehensive Developmental Neuroscience, Volume 3. Elsevier, Oxford.

Sporns, O., 2011. Networks of the Brain. MIT Press, Cambridge, MA.

Steele, C., 1997. A threat in the air. How stereotypes shape intellectual identity and performance. American Psychologist 52, 613–629.

Steinberg, L., 2008. A social neuroscience perspective on adolescent risk-taking. Developmental Review 28, 78–106.

Stevens, J.S., Hamann, S., 2012. Sex differences in brain activation to emotional stimuli: A meta-analysis of neuroimaging studies. Neuropsychologia 50, 1578–1593.

Stiles, J., Akshoomoff, N., Haist, F., 2013. Spatial cognition. Neural Circuit Development and Function in the Healthy and Diseased Brain: Comprehensive Developmental Neuroscience, Volume 3. Elsevier, Oxford.

Su, R., Rounds, J., Armstrong, P.I., 2009. Men and things, women and people: A meta-analysis of sex differences in interests. Psychological Bulletin 135, 859–884.

Thambisetty, M., Wan, J., Carass, A., An, Y., Prince, J.L., Resnick, S.M., 2010. Longitudinal changes in cortical thickness associated with normal aging. NeuroImage 52, 1215–1223.

Thomas, J.R., French, K.E., 1985. Gender differences across age in motor performance: A meta-analysis. Psychological Bulletin 98, 260–282.

Thompson, P.M., Giedd, J.N., Woods, R.P., MacDonald, D., Evans, A.C., Toga, A.W., 2000. Growth patterns in the developing brain detected by using continuum mechanical tensor maps. Nature 404, 190–193.

Thomsen, T., Hugdahl, K., Ersland, L., et al., 2000. Functional magnetic resonance imaging (fMRI) study of sex differences in a mental rotation task. Medical Science Monitor 60, 1186–1196.

Tracy, D.M., 1990. Toy-playing behavior, sex-role orientation, spatial ability, and science achievement. Journal of Research in Science Teaching 27, 637–649.

Uttal, D.H., Meadow, N.G., Tipton, E., et al., 2012. The malleability of spatial skills: A meta-analysis of training studies. Psychological Bulletin.

van den Heuvel, M.P., Stam, C.J., Kahn, R.S., Pol, H.E.H., 2009. Efficiency of functional brain networks and intellectual performance. Journal of Neuroscience 29, 7619–7624.

Vasta, R., Liben, L.S., 1996. The water-level task: An intriguing puzzle. Current Directions in Psychological Science 5, 171–177.

Vawter, M.P., Evans, S., Choudary, P., et al., 2004. Gender-specific gene expression in post-mortem human brain: Localization to sex chromosomes. Neuropsychopharmacology 29, 373–384.

Vogel, J.J., Bowers, C.A., Vogel, D.S., 2003. Cerebral lateralization of spatial abilities: A meta-analysis. Brain and Cognition 52, 197–204.

Voyer, D., 2011. Sex differences in dichotic listening. Brain and Cognition 76, 245–255.

Voyer, D., Bryden, M.P., 1993. Masking and visual field effects on a lateralized rod-and-frame test. Canadian Journal of Experimental Psychology 47, 26–37.

Voyer, D., Nolan, C.L., Voyer, S., 2000. The relation between experience and spatial performance in men and women. Sex Roles 43, 891–915.

Voyer, D., Postma, A., Brake, B., Imperato-McGinley, J., 2007. Gender differences in object location memory: A meta-analysis. Psychonomic Bulletin and Review 14, 23–38.

Vul, E., Harris, C., Winkielman, P., Pashler, H., 2009. Puzzlingly high correlations in fMRI studies of emotion, personality, and social cognition. Perspectives on Psychological Science 4, 274–290.

Vuoksimaa, E., Kaprio, J., Kremen, W.S., et al., 2010. Having a male co-twin masculinizes mental rotation performance in females. Psychological Science 21, 1069–1071.

Wager, T.D., Phan, K.L., Liberzon, I., Taylor, S.F., 2003. Valence, gender, and lateralization of functional brain anatomy in emotion: A meta-analysis of findings from neuroimaging. NeuroImage 19, 513–531.

Wai, J., Cacchio, M., Putallaz, M., Makel, M.C., 2010. Sex differences in the right tail of cognitive abilities: A 30 year examination. Intelligence 38, 412–423.

Wallen, K., 1996. Nature needs nurture: The interaction of hormonal and social influences on the development of behavioral sex differences in rhesus monkeys. Hormones and Behavior 30, 364–378.

Wallen, K., 2005. Hormonal influences on sexually differentiated behavior in nonhuman primates. Frontiers in Neuroendocrinology 26, 7–26.

Wallen, K., 2009. The organizational hypothesis: Reflections on the 50th anniversary of the publication of Phoenix, Goy, Gerall, and Young (1959). Hormones and Behavior 55, 561–565.

Wallentin, M., 2009. Putative sex differences in verbal abilities and language cortex: A critical review. Brain and Language 108, 175–183.

Weisberg, D.S., Keil, F.C., Goodstein, J., Rawson, E., Gray, J.R., 2008. The seductive allure of neuroscience explanations. Journal of Cognitive Neuroscience 20, 470–477.

Weiss, E., Siedentopf, C.M., Hofer, A., et al., 2003a. Sex differences in brain activation pattern during a visuospatial cognitive task: A functional magnetic resonance imaging study in healthy volunteers. Neuroscience Letters 344, 169–172.

Weiss, E.M., Siedentopf, C., Hofer, A., et al., 2003b. Brain activation pattern during a verbal fluency test in healthy male and female volunteers: A functional magnetic resonance imaging study. Neuroscience Letters 352, 191–194.

Witte, A.V., Savli, M., Holik, A., Kasper, S., Lanzenberger, R., 2010. Regional sex differences in grey matter volume are associated with sex hormones in the young adult human brain. NeuroImage 49, 1205–1212.

Wood, W., Eagly, A.H., 2002. A cross-cultural analysis of the behavior of women and men: Implications for the origins of sex differences. Psychological Bulletin 128, 699–727.

Wraga, M., Helt, M., Jacobs, E., Sullivan, K., 2007. Neural basis of stereotype-induced shifts in women's mental rotation performance. Social Cognitive and Affective Neuroscience 2, 12–19.

Zahn-Waxler, C., 1993. Warriors and worriers: Gender and psychopathology. Development and Psychopathology 5, 79–89.

Zahn-Waxler, C., Shirtcliff, E.A., Marceau, K., 2008. Disorders of childhood and adolescence: Gender and psychopathology. Annual Review of Clinical Psychology 4, 275–303.

Zhang, K., Sejnowski, T.J., 2000. A universal scaling law between gray matter and white matter of cerebral cortex. Proceedings of the National Academy of Sciences of the United States of America 97, 5621–5626.

Zhou, J.N., Hofman, M.A., Gooren, L.J.G., Swaab, D.F., 1995. A sex difference in the human brain and its relation to transsexuality. Nature 378, 68–70.

Zilles, K., Armstrong, E., Schleicher, A., Kretschmann, H.J., 1988. The human pattern of gyrification in the cerebral cortex. Anatomy and Embryology 179, 173–179.