**Introduction**

Behavioral maturation is a major part of adolescence that, together with the many concomitant physical changes of puberty, transforms children into young adults. Because the outcomes represent the future of the society, virtually every group on record attempts to manage the process to achieve desired goals. Ethnographic and historical accounts document a wide variety of strategies to guide and influence adolescent development, from structured formal interventions (rituals, schools) to age/stage-specific activities and expectations (labor and task assignment, recreational options, skills attainment), to adjustment of daily settings (living arrangements, apprenticeship, altered supervision/monitoring, exposure to peers). These situations and demands may or may not mesh with individual inclinations and abilities, and the resulting tensions and strains on adults and the adolescents themselves not infrequently lead to adult perceptions of adolescents as unruly and difficult. Thus, the discovery of hormones and their role in puberty during the early–mid twentieth century fostered a popular attribution of the emotional–behavioral turmoil around adolescence to ‘raging hormones.’

The insight that adolescence is a stressful period of heightened vulnerability has emerged more recently. Even as the adolescent confronts new demands, capacities, and expectations, the maturation processes of physical (growth, reproductive) and cognitive-emotional systems themselves are not fully synchronized and proceed on different schedules. Gaps among

---

**Hormones and Behavior**

C M Worthman, Emory University, Atlanta, GA, USA

© 2011 Elsevier Inc. All rights reserved.

---

**Glossary**

**Hormones:** Chemicals produced in the body at one location (usually a gland such as the adrenal, ovary, or testis) which produce an effect on the activity of another location, called the target tissue. Target tissues have receptors where the hormone binds to generate a sequence of cellular responses. Most but not all hormones are transported through the body via the bloodstream.

**Limbic system:** A set of loosely defined structures located around the border of the cortex in the ancient core of the brain, including the hippocampus, amygdala, fornix, cingulate gyrus, and hypothalamus, among others. Structures in this group have connections to regions throughout the brain and are associated with emotion and affective processing, long-term memory formation, behavior, and endocrine and autonomic regulation.

**Prefrontal cortex:** The frontal lobes is a core area for high-level processing that integrates internal states (sensory information, affective processing), with thoughts and intentions to make decisions and guide actions. During adolescence, this region undergoes distinct maturational changes involving growth, pruning, and hence reorganization.

**Steroid hormones:** A class of small compounds whose distinctive structure permits them to move directly through membranes and whose powerful actions are due to their capacity to alter gene transcription in the nucleus of cells in target tissues. They include gonadal (testosterone, estradiol) and adrenal (cortisol, adrenal androgens) secretions involved, among other things, in reproduction and stress responses.

**Stress reactivity:** The cognitive-emotional and associated neuroendocrine sensitivity to stressors. High reactivity is linked to greater endocrine and autonomic stress responsiveness that increase the strength and duration of hormonal (cortisol) and physical (heart rate) reactions to stress. As such, reactivity reflects the psychological and physiological impact of stressors on an individual.

---

**Abbreviations**

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTH</td>
<td>Adrenocorticotropic hormone</td>
</tr>
<tr>
<td>CRF/CRH</td>
<td>Corticotrophin releasing factor/hormone</td>
</tr>
<tr>
<td>DALY</td>
<td>Disability-adjusted life years</td>
</tr>
<tr>
<td>DHEA</td>
<td>Dehydroepiandrosterone</td>
</tr>
<tr>
<td>DHEAS</td>
<td>Dehydroepiandrosterone sulfate</td>
</tr>
<tr>
<td>DNA</td>
<td>Deoxyribose nucleic acid</td>
</tr>
<tr>
<td>FSH</td>
<td>Follicle stimulating hormone</td>
</tr>
<tr>
<td>GH</td>
<td>Growth hormone</td>
</tr>
<tr>
<td>GHRH</td>
<td>Growth hormone releasing hormone</td>
</tr>
<tr>
<td>GnRH</td>
<td>Gonadotropin releasing hormone</td>
</tr>
<tr>
<td>HPA</td>
<td>Hypothalmo–pituitary–adrenal axis</td>
</tr>
<tr>
<td>HPG</td>
<td>Hypothalamo–pituitary–gonadal axis</td>
</tr>
<tr>
<td>HPT</td>
<td>Thyrotropic or hypothalmo–pituitary–thyroid axis</td>
</tr>
<tr>
<td>IGF-1</td>
<td>Insulin-like growth factor</td>
</tr>
<tr>
<td>LH</td>
<td>Luteinizing hormone</td>
</tr>
<tr>
<td>NPY</td>
<td>Neuropeptide-Y</td>
</tr>
<tr>
<td>POMC</td>
<td>Pro-opiometanocortin</td>
</tr>
<tr>
<td>SRIF</td>
<td>Somatotropic hormone releasing-inhibiting factor, or somatomedin</td>
</tr>
<tr>
<td>STA</td>
<td>Somatotropic axis</td>
</tr>
<tr>
<td>T4</td>
<td>Thyroxine</td>
</tr>
<tr>
<td>TRH</td>
<td>Thyroid releasing hormone</td>
</tr>
<tr>
<td>TSH</td>
<td>Thyroid stimulating hormone</td>
</tr>
</tbody>
</table>
physical, emotional, cognitive, and behavioral attainments complicate the process of adolescent adjustment. The most obvious and dramatic changes in body morphology (size and shape), physiology, and behavior relate to reproductive maturation, leading to a focus on the role of gonadal hormones in these transformations. Hence, much of the early work on hormones and behavior in adolescence focused on the hormones involved in reproductive maturation, particularly the so-called ‘sex hormones,’ testosterone and estradiol. But recognition that the hormones of stress may be intimately involved with adolescent behaviors has been informed by growing evidence of the role of activity and stress reactivity of the stress response system in adolescent social cognition and behavior.

This survey commences by reviewing why the psychobehavioral health of adolescents is of particular importance today. The following sections explain the regulation and developmental course of hormones of significance in puberty and adolescence. To streamline the enormous complexity of the neuroendocrine system, discussion will focus on three key elements of adolescent maturation: reproduction (the gonads), stress (adrenals), and affective-cognitive processing (brain). The term ‘neuroendocrine’ here recognizes the fact that the nervous and endocrine systems essentially form a functional unit. The dynamics of hormones and behavior in adolescence must be understood to operate within a network of interacting developmental, physiological, perceptual, and social forces. A heuristic model of these developmental biosocial dynamics is provided to walk the reader through the complexities. Then, translation of the insights gained from hormone-behavior dynamics for addressing the practical problem of adolescent mental health is applied to the urgent matter of depression. A consideration of the implications for global youth concludes the discussion.

A Brief Global Epidemiology of Adolescence

Youth are the cornerstones of any society’s future, and this is especially true today. Recent trends have created a demographic bind. On the one hand, human population expansion has created the largest global cohort of youth ever seen, comprising over one billion aged 15–24 plus 1.2 billion aged 5–14 in a total human population of over 6.5 billion in 2005. On the other hand, increased longevity and declining fertility have contributed to population aging and diminished the global proportion of young people. Matters concerning youth therefore assume dual importance, for the sheer numbers and human potential youth represent, and for their future significance in aging populations.

Whatever the demographics, understanding youth behavior is critical because the major threats to their health during this period have their origins in behavior rather than infectious or chronic disease. Mortality is at its lowest in the teen and young adult years, but the rapid physical and psychobehavioral changes of puberty and adolescence alter the risks of health-related behavior problems, including sexual and physical risk-taking, substance use, suicide, and mood disorders. The age distribution of the burden of morbidity and mortality (expressed in terms of disability-adjust life years, Figure 1) reveals that rates of injury and insult are at their highest during the period of late adolescence and early adulthood, exceeded only by the high burden of insult associated with birth and malnutrition in infancy. Note also that the burden of communicable disease increases by 50% and that from noncommunicable diseases triples between ages 5–14 and 15–29. Behavior plays key roles in these expansions to burden. For instance, rates of suicide increase dramatically, particularly in young men. The rising importance of romantic and peer relationships contributes to sexual risk-taking with consequences for reproductive health such as sexually transmitted diseases or premature childbearing. Sensation seeking and initiation of substance use contribute to increasing rates of accidents. A pressing question has been why youth are prone to behaviors that risk their present and future welfare, and where the key points of leverage may lie to optimize successful, healthy pathways through adolescence.

Another special historical circumstance is relevant. As a group, global youth today are physically maturing earlier than perhaps any time in human history, owing to widespread improvements in health and nutrition. It also appears that early-maturing populations such as those in Europe, the United States or Japan progress through puberty more rapidly than their later-maturing ancestors and contemporaries. Consequently, the association of earlier exposure to the physiological and bodily changes of puberty to the ongoing neurocognitive and behavioral maturation of adolescents remains an important but unresolved question. Do the accelerated timing and pace of puberty fuel a growing mismatch between physical and psychosocial development? How and how much are physiological and neurocognitive maturation synchronized at puberty, and what is the role of social expectations, constraints, and opportunities in producing asynchronies between

---

**Figure 1** Distribution of the burden of disease by source across age groups under age 60 years. Burden is calculated in terms of disability-adjusted life-years (DALYs). Based on data in Mathers and colleagues (2006, Table 3C9, pp. 228–233). Sources of burden: communicable disease (gray), insult (black), noncommunicable disease (white), and injury (dotted).
physical and psychosocial maturation? Puberty brings a final phase of growth and the beginning of the adult productive and reproductive career with concomitant demands on forming and conducting social relationships, performing social roles, and making effective and responsible decisions. Thus, the connection of physical and psychosocial maturation is a critically important one.

**Hormones in Developmental Processes**

The key purpose of hormones is to make things happen. Hormones by definition are secreted in one place to have an effect on another. Thus, hormones mediate short-term projects such as digesting a meal, as well as long-term ones such as growing up or having a baby. Understanding about the role of hormones in behavioral maturation at adolescence is evolving along with insights about sites and mechanisms of endocrine action, the impact and mediation of experiential effects, and processes of brain maturation. To understand the effects of endocrine changes during this period requires a view of puberty as part of an ongoing process of development that begins in utero. During gestation and the first few postnatal months, hormones influence the structure of neural pathways in the brain that will form the basis of behavior regulation. Such irreversible effects on structure and shaping of adult behavior comprise the organizational effects of hormone action, which may not be expressed until later exposure to the hormones produced in puberty. Reversible endocrine stimulation of behavior expression comprises the activational effects of increased hormonal outputs. Much of the work on organizational effects has focused on the possible action of gonadal steroid hormones in mediating sex differences in behavior via their early organizational effects on the brain, followed by activational effects in puberty and adulthood. Now, however, imaging studies of brain development strongly suggest that the brain undergoes an adolescent period of growth and reorganization that is subject to organizational effects by hormones as well.

**Overview of Endocrine Regulation and Production**

To understand hormone–behavior interactions, first it is useful to review endocrine regulation and production within the neuroendocrine continuum. The four classic endocrine systems outlined in **Figure 2** establish dynamic feedback between the brain and the body’s endocrine activity via a three-step process involving the hypothalamus, pituitary, and target organ. The brain produces releasing hormones (CRH, GnRH, GHRH/SRIF, TRH) from the hypothalamus that trigger secretion of hormones from the pituitary (ACTH, LH and FSH, GH, and TSH) that in turn stimulate production of cortisol, gonadal steroids testosterone and estradiol, IGF-1, and T4. Circulating levels of these hormones provide feedback to the brain about target organ activity, and releasing hormone production is adjusted accordingly. These four pathways are known respectively as the hypothalamo–pituitary–adrenal (HPA), hypothalamo–pituitary–gonadal (HPG), somatotropic (STA), and thyrotropic or hypothalamo–pituitary–thyroid (HPT) axes. More recently, the importance of distributed endocrine activity that has central nervous system effects has been recognized, such as the production of leptin by white fat or of cytokines by lymphocytes. The HPG axis shows the most dramatic changes during puberty, but the STA is also involved in the growth spurt and likewise, the HPA exhibits alterations in its activity.

![Figure 2](image-url)  
**Figure 2** Overview of classic endocrine systems. These four endocrine systems represent functional axes that each operate via a three-step process involving the hypothalamus, pituitary, and target organ. More recently, the importance of distributed endocrine activity that has central nervous system effects has been recognized, such as the production of leptin by white fat or of cytokines by lymphocytes.
Developmental Trajectories

The reproductive axis
During gestation, gonadal activity plays a key role in sex differentiation. Specifically, morphological and functional sex differentiation is triggered by an early cascade of genetic factors and the reproductive axis becomes functional, reaching adult levels of gonadotropins by mid-gestation and declining thereafter until after birth, when they rise again during the first year of life. Similarly, the gonads actively produce testosterone or estradiol during gestation and show another surge during the first months after birth. The axis becomes quiescent in the second year, and remains so until nighttime pulses in gonadotropins signal the onset of puberty. Gonadotropin production mediates brain regulation of the reproductive axis but it is the gonadal steroids they stimulate that exert organizational and activational effects on the brain and the body.

How does the body know when to begin puberty? Answering that question could net a Nobel Prize. This biological puzzle is important because puberty is triggered by distinct but elusive neuroendocrine mechanisms that act as the pace makers of human development. The mechanisms are necessary because the systems regulating reproductive maturation have been profoundly suppressed to create the distinctively human phenomenon of prolonged childhood. Something must reverse the decade-long quiescence to close the childhood phase and permit the final stages of maturation to proceed. A suite of permissive factors (nutritional status, stress, physical health) modulates pubertal timing, but nevertheless the pace maker appears to be located in the central nervous system. Girls enter puberty slightly earlier than boys and experience rises in estradiol reflecting ovarian activation that gradually reaches levels sufficient to establish ovarian cyclicity. Menarche is an early marker of such cyclicity, but it takes years for the axis to achieve routine ovulation and robust, stable ovarian cycles. Males, by contrast, experience systematic increases in testosterone and attain adult levels in mid-late puberty. However, the external signs of maturation (voice change, beard growth) appear only at sustained, well-elevated levels of testosterone and thus they manifest relatively late in puberty.

The adrenals
The dramatic changes attending reproductive maturation claim attention, yet another system undergoes similarly dramatic endocrine changes whose biological effects remain relatively cryptic. The adrenals are intensely active during gestation, supplying most of the endocrine support for placental activity to regulate fetal and maternal metabolism and exchange. After birth, they undergo a period of reorganization. Both gestation and the early years appear to be sensitive periods for HPA organization during which maternal stress, maltreatment, and trauma alter basal activity and reactivity of the axis. Diurnal patterns of cortisol production, as well as sensitivity of the HPA axis to challenge, are established during the first year of life. During adolescence, the HPA undergoes age- and puberty-related increases in basal levels of cortisol as well as changes in stress reactivity. Although reactivity tends to increase during adolescence and move toward an adult pattern of HPA response to stressors, both sexes exhibit hyporesponsiveness around age 11, followed by marked sex differences around age 13 when boys remain nonreactive and girls become hyperreactive. Current evidence suggests these changes are more closely related to age than to pubertal status.

The HPA axis is essentially an on-demand system that mobilizes the body's response to challenges. HPA responsivity to challenge, in terms of how much cortisol is released and for how long, is a key feature that is determined by both psychological and biological factors. Appraisal of the stressor provides the trigger for HPA response: the more intense the internal perception of challenge, the greater the HPA response. But the HPA axis itself may be more or less responsive to stimuli or regulatory feedback that alters the strength and duration of cortisol release. Given these sources of individual variability, HPA reactivity to challenge has been used as an important index of functional regulation of the axis and the burden of stressors under everyday conditions for each individual.

Weak androgens are another set of adrenal hormones (see Figure 2), the most prominent of which is DHEA and its sulfated form, DHEAS. These have a distinctive developmental trajectory. DHEA/S rise postnatally and then decline to low levels during the second year. They then increase slightly yet distinctly at adrenarche, between ages 6 and 8. The onset of puberty is paralleled by a more rapid ascent that continues until around age 25, so that DHEAS becomes by far the most prevalent form of circulating steroid hormone. The regulation of adrenal androgens is not entirely clear, nor is their function (at puberty, they stimulate growth of axillary and pubic hair), yet their profile of developmental change is remarkably pronounced across the life course. The developmental course of DHEA/S production is independent of the reproductive axis: when adrenarche was discovered nearly 40 years ago, some thought it may be a preliminary phase of puberty, but clinical evidence has established that the two are dissociated. DHEA/S is implicated in widespread neuromodulatory and neuroprotective actions, and a small literature finds tenuous links to risk for mood and behavior problems in adolescents that will not be reviewed here.

Hormone-Behavior Interactions in Puberty and Adolescence

Historically, western science and society have characterized adolescence as a difficult period of unrest, unruliness, exploration, and risk-taking that causes anxiety for parents and alarm among the guardians of authority and the status quo. ‘Raging hormones’ – more specifically, ‘sex’ hormones produced by activating gonads – often have been pegged as the cause of teen tension and trouble and thus, these difficulties are regarded as endemic to puberty itself. Gonadal hormones often have been found guilty by association because dramatic behavior changes appear to coincide with surges in their production, going from virtually zero in late childhood to adult levels in mid-late adolescence. But this logic has unraveled in the face of mounting evidence. The major changes in behavior and behavior problems occur after puberty starts. Moreover, direct correlations between hormone levels and behavior are rarely found. Nevertheless, pubertal hormones are known to have organizational and activational effects on the neuroregulation of emotion, but the pathways by
which these effects are manifested involve social–experiential factors as well.

Other complexities cloud the ability to link behavioral changes of adolescence to the neuroendocrine changes of puberty. During this time, the activity and architecture of several neuroendocrine systems undergo maturation, production of multiple hormones is altered, the patterns of endocrine activity (not just the average) determine its physiological significance, and individuals vary enormously in timing, course, and extent of change. Both early organizational effects and genetic background contribute to this variation. Recall, too, that the processes of maturation occur on somewhat different schedules and are either partially synchronized or largely independent of one another. Furthermore, pubertal changes both affect and are affected by the contexts in which they occur.

**An Integrative Biosocial Approach**

Thus, developmental science has come to regard hormone–behavior interactions in adolescence as participating in a network of contributory factors, rather than as a simple cause–effect relationship. A heuristic model of these complexities is provided in Figure 3, using the example of gonadal steroids. If we are to understand the connections between endocrine change and psychobehavioral outcomes, at least several candidate pathways must be considered. First is endocrine mediation, whereby maturational processes activate the GnRH pulse generator that in turn drives gonadotropin release to increase output of testosterone and/or estradiol. These hormones then moderate neurological mechanisms involved in behavior and behavior regulation, including an influence on the structures involved in social cognition and emotion regulation. This chain of events comprises what have been regarded as the activational effects of gonadal steroids. Second, another possibility is central mediation, namely, the same maturational processes that trigger the onset of puberty also involve alterations in the central mechanisms organizing behavior independent of gonadal maturation. Logically, it could also be that gonadotropins themselves exert effects on these mechanisms, although there is no evidence supporting that link. Recent brain imaging does, however, support the importance of a central pathway via adolescent maturation of the brain itself. Third is maturational cuing: body changes signaling pubertal status alter self perceptions, expectations, and evaluations. In addition, changing appearance affects perceptions and responses in social contexts and existing relationships that set up both positive (opportunity) and negative (challenge) stressors. Novel stressors, in turn, directly affect social cognition and emotional-evaluative processes. These cognitive-evaluative processes mediate the impact of each avenue of maturational cuing on the central regulation of behavior. Social mediation comprises the fourth pathway, whereby social contexts and relationships produce opportunities, demands, and stressors that directly influence the central regulation of behavior. This pathway recognizes the important role of norms, relationships, and contexts in adolescent behavior and behavior changes, independent from hormones per se.

All of these pathways operate in concert, so the question has become how they work together and what determines the relative contributions of one pathway or another. A critical dimension not represented in this model is time: puberty and adolescence are framed within ongoing developmental processes that extend from conception through aging. Thus, what happens during this time is shaped by prior experience and development while it also shapes future social and physical trajectories through adulthood.

**Central Mediation**

Brain maturational changes in the second decade play a major role in the behavioral changes observed in adolescence. Innovative technologies for imaging brain structure and activity have opened new windows onto brain architecture and activity that are revolutionizing understandings of its development as well as of brain function and its roles in cognition and behavior. At birth, the human brain is relatively large and grows much more rapidly than does the rest of the body, attaining 50% of adult size by age 1 and 95% by age 10. However, growth in size is only a small part of brain development, which mainly involves the structuring and restructuring of anatomical arrangements within the brain. Connectivity is a major determinant of how the brain operates, so processes that shape how cells and regions of the brain talk with each other comprise the most powerful determinants of mature function. Prominent aspects of these processes are pruning and myelination. Pruning is the removal of nerve connections (synapses) or neurons to sculpt fine and large patterns of connectivity among neurons. Myelination most simply may be thought of as the process of insulating the wiring of the
brain to enhance both speed and specificity of connections among brain regions. Together, pruning and myelination represent potent means of shaping patterns of activity and transmission, and hence function.

During development, neuronal and synaptic overproduction and pruning drive structure, while myelination matures transmission speed. The number of unmyelinated neurons, or gray matter, expands rapidly in fetal and infant development and then undergoes pruning in a dynamic ‘use it or lose it’ process whereby synapses (nerve connections) and neurons that are exercised or activated are retained. Those that do not ‘work’ expire. Recent imaging studies have revealed another wave of gray matter overproduction in early puberty, at age 11 in girls and 12 in boys, followed by some thinning. A thickening of cortical gray matter indicates the production of new nerve cells, while cortical thinning reflects the maturational processes of pruning and myelination that sculpt regional and overall brain functioning. Such thickening and then thinning of the cerebral cortex happens at different times in adolescent development for different functional areas, but occurs primarily in the frontal lobe, a region responsible for ‘executive functions’ such as reasoning, planning, and impulse control. Myelination of neuronal fibers and tracts is progressive and proceeds from the front to the back of the brain, as reflected in the expansion of white matter that commences in early childhood and attenuates after age 12. However, the frontal lobes also show another phase of myelination during the teen years, which is thought to support maturation of cognition and executive functions, although development of sensory, auditory, language, and spatial functions is largely complete. Overall, then, anatomical changes in the brain, represented in part by gray matter decreases and white matter increases, provide clear evidence that adolescence is an important period of brain development.

In sum, adolescence is a phase of extensive brain development that involves several systems and changes in synaptic density and myelination. These processes are particularly evident in the frontal lobes; indeed, the prefrontal cortex is the latest area of the brain to develop mature synaptic density and myelination. Additionally, limbic structures involved in affect and memory develop during adolescence, manifested most notably in increasing volume of the amygdala and hippocampus. These maturational patterns have important implications for understanding adolescent affective-behavioral attainments and vulnerabilities. Executive function, or the ability to implement rational analysis and planned intentions and to manage countervailing feelings and impulses in the control of behavior, is particularly challenging for adolescents. This is not just a matter of maturation in specific brain regions, but also of consolidation of tracts linking different regions of the brain to facilitate and coordinate complex, timely processing and behavior regulation. The collaborative function of different brain regions that is seen in adults is not yet formed in adolescents, whose brains literally must work harder to accomplish such tasks. In part, this is due to the apparent asynchrony in the emergence at puberty of affective-appetitive drives and the development of cognitive-regulatory systems. For example, the amygdala plays a central role in affective processing and managing the dynamics between emotion and cognition, and is critical to memory consolidation. Interactions between the prefrontal cortex and the amygdala produce the assignment of emotional valences to facial expressions, and adolescents show a series of shifts in such processing. Maturation of amygdala–prefrontal connections may underlie the dramatic social and emotional changes in early adolescence.

**Endocrine Mediation**

For hormones to affect behavior, they must influence brain activity, directly or indirectly. Steroid hormones such as estradiol, testosterone, or cortisol are particularly potent because they can pass directly through membranes to exert their effects within the cell, at the level of gene expression. Target tissues contain cellular receptors that act as transcription factors: these receptors bind the steroid, transport it to the nucleus, and directly regulate DNA transcription. The distribution and density of receptors determine the sites, specificity, and intensity of endocrine action. Thus, for example, in emotion regulating regions of the brain such as the hippocampus, cortisol binds to two classes of receptors (mineralocorticoid and glucocorticoid) that mediate its concentration-dependent actions. In another example, testosterone exerts its actions indirectly in some tissues through its aromatization to estradiol and binding to estrogen receptors within the target tissue.

The brain is richly furnished with steroid receptors. There are two major recognized estrogen receptors, the alpha-receptors concentrated in the hippocampus and connecting regions, beta-receptors scattered throughout the brain including cerebral cortex, plus a membrane receptor, G protein-coupled estrogen receptor (GPR30), concentrated in the hypothalamus and pituitary. Several other proteins also are known to bind estrogen to create a diverse array of estrogen-mediated effects throughout the body. The androgen receptor binds testosterone; its distribution in the brain largely overlaps that of the estrogen receptors. Estrogen receptors are important sites for testosterone action in cells that convert it to estradiol. Glucocorticoid receptors, on the other hand, are found throughout the brain, and particularly in the hippocampus, amygdala, and frontal cortex.

**Gonadal steroid hormones**

The emergence of sexual and sex-specific reproductive behaviors during puberty and adolescence is a central and dramatic feature of this developmental period. Accordingly, early endocrine research focused on the roles of gonadal steroid hormones (especially estradiol, testosterone, and progesterone) in reproductive function and behavior, and gender differences in cognition and behavior. But the activities of these hormones extend much further than that, and the equation of gonadal steroid action with sex (testosterone in men, estradiol in women) has eroded with recognition of the roles of both hormones in either sex. Throughout development and adulthood, gonadal steroid hormones play active regulatory roles in shaping neuronal architecture and function. These hormones influence a wide range of neurodevelopmental processes, from dendritic growth, cell death, and synaptic formation and elimination, to expression of neuropeptides and receptors. The activity of several neurotransmitter systems (including dopaminergic, serotonergic, cholinergic, and...
noradrenergic neurons) is modulated by gonadal steroid hormones. These systems play key roles in the regulation of higher-order functions that inform behavior, such as cognition and emotion regulation. Several of them, as well as others regulated by gonadal steroids (oxytocin, vasopressin, endogenous opioids), are directly involved in social responsiveness. The actions of gonadal steroid hormones are particularly evident in the limbic system (amygdala, hippocampus, striatum), cerebellum, and cortex and influence many behaviors, such as verbal, motor, and spatial abilities, aggression, emotion regulation, and some dimensions of learning and memory. For example, sex differences in fear conditioning are associated with attenuation in women by estrogen suppression of long-term potentiation in the hippocampus. Similarly, the amygdala has a high concentration of androgen receptors and shows sex differences in its activation patterns: activation to angry faces correlates with circulating testosterone in men but not in women.

Pubertal increases in gonadal steroid hormones change the processing of social experience. Strong specific effects of gonadal steroids on target brain regions include sexual behavior, social bonding, and social memory. Given the pattern of receptors and target tissues, it is unsurprising that emotional and behavioral responsiveness to social stimuli constitutes an important arena of gonadal steroid hormone influence at adolescence. For instance, in both females and males, sexual responsiveness to a social stimulus is enhanced with increased circulating androgen levels. Adolescents characteristically manifest heightened self-awareness and sensitivity to peer acceptance and rejection. Gonadal steroid hormones, particularly androgens, also have been linked to social dominance and status-seeking behaviors. Some animal models indicate that these endocrine effects are greatest during early encounters with a novel stimulus, suggesting a basis for the formation of patterns of social behavior during adolescence.

Recent imaging studies are beginning to reveal links of brain development with endocrine and other pubertal changes. Amygdala volume increases in boys but decreases in girls with pubertal progression as indexed by testosterone levels. However, cortical thinning is greater with increasing testosterone in girls but not boys. Interactions between the amygdala, critical for processing emotional information, and frontal cortical regions important for risk evaluation and impulse control may follow different courses in females and males during puberty-related brain development. If a thinner cortex is related to better executive control over the emotional processing centers of the amygdala, then this helps explain differences in emotional processing between boys and girls, depending on pubertal status and brain maturation. Adolescents also exhibit alterations in reward-related behavior that are thought to contribute to increasing emotional and behavioral problems such as mood disorders and drug abuse.

Brain imaging studies have reported conflicting results about adolescent maturational change in reactions to experience by reward-related structures such as the striatum and medial prefrontal cortex (mPFC). One argument points to evidence of increased activation to suggest that rewards are more salient to adolescents, which enhances reward-related brain activation and thence greater reward-seeking behavior. Another argument points to evidence of reduced reward-related brain reactivity and suggests a blunted response to reward among adolescents that, in turn, motivates them to seek more rewarding experiences in order to maintain reward circuit activity at an optimal level. A recent imaging study by Forbes and colleagues examined the association of reward-related brain function to everyday real-world experience, and found that reward-related brain function changes with puberty and is associated with positive affect and depressive symptoms. Specifically, testosterone correlated negatively with reward-related brain reactivity to receipt of reward; hence, increased reward-seeking in adolescence may act to compensate for these changes.

**Glucocorticoids**

Appropriate levels of glucocorticoids (cortisol is the dominant form in humans), neither high nor low, are necessary for normal brain development. But glucocorticoid levels are highly responsive to stressors, particularly psychosocial stress. Thus, the timing of exposure to stressors directly influences their impact on the developmental course of HPA function and on glucocorticoid-sensitive structures (hippocampus, frontal cortex, amygdala) involved in affective, cognitive, and behavioral regulation. During gestation, glucocorticoids are involved in shaping brain architecture (e.g., neuronal remodeling, myelination, glial maturation). In accord with the animal literature, prenatal stress (maternal stress, depression, adversity, or treatment with glucocorticoids) results in fetal programming of the HPA and persistently increased basal HPA activity. Such prenatal adversity has been linked to perturbations in neurological, cognitive, and behavioral development that include social insensitivity, sleep disturbance, and attention deficit hyperactivity disorder, along with increased risk for psychiatric problems such as substance abuse and mood and anxiety disorders.

Converging lines of evidence in animals and humans point to the importance of early caregiving quality for establishing HPA regulation that is robust to everyday challenges. Responsive and sensitive parenting provides social regulation of infant HPA development, while early harsh conditions conduce to dysregulated HPA activity. Such effects appear to be enduring and affect later functioning. For example, increased HPA activity in adolescents whose mothers suffered from postpartum depression is responsible for the association between early adversity and late depressive symptoms. Recent evidence suggests a particular sensitivity of the adolescent brain to elevated glucocorticoids and thus to stress. This sensitivity is greatest in the frontal cortex, where development is proceeding apace. Gene expression studies have found that levels of glucocorticoid receptor mRNA in the prefrontal cortex are high in adolescents compared to earlier and older age groups. Additionally, the effects of early adversity on HPA function may also emerge in adolescence as youth face developmental stressors inherent to that maturational period. Thus, girls born with low birthweight who then experience childhood adversity show both greater cortisol reactivity and risk for depression at adolescence.

HPA activation is most reliably linked to two conditions, social challenge/threat and perceived lack of control. The increased salience of social stimuli and heightened emotional reactivity, along with all the physical changes, are each promoted by surging gonadal steroids and contribute to increased adolescent self-consciousness and hypersensitivity to peer
relations. Such sensitivities activate the HPA and likely contribute to the greater HPA stress reactivity that adolescents experience. Individual differences in cognitive- affective responses to stressors can further exacerbate the burden of stress, and here the effects of prior experience and predispositions come into play. Heightened HPA activity in adolescence also has a bearing on HPG actions, because glucocorticoids have suppressive effects on HPG function at the level of the brain and gonads. Stress responsiveness is gender (social) and sex (biological) differentiated and merits much more study. At birth, HPA regulation differs in males and females, the ACTH: cortisol ratio being greater in infant boys, and sex differences in responses to stress persist. HPA response to stressors like public speaking or mental arithmetic is greater in males than females, and is also moderated by partner support in males but not females. HPA reactivity is more sensitive to social rejection in women and to achievement challenges in men, especially in youth. The role of sex and gender differences in exposure and responses to different stressors during adolescence remains underexplored. Acute or chronic psychosocial stress can disrupt the reproductive axis and delay puberty and maturation. Interactions of gonadal steroid hormones and glucocorticoids may contribute to the complexities of psychobehavioral changes and vulnerabilities during adolescence.

Maturational Cuing

The pathbreaking ability to image brain structure and function along with techniques for minimally invasive hormone sampling have drawn scientific attention away from earlier foci on psychological and social processes mediating pathways between puberty and behavior. Self as well as peer perceptions of maturational status also play a role in forging these pathways. The bodily changes of puberty that visibly manifest the maturational status also play a role in forging these pathways. The bodily changes of puberty that visibly manifest the maturational status of the adolescent also mobilize self- and other-expectations for new behaviors, competencies, relationships, and statuses to be performed and mastered. Earlier studies relied on morphologic changes to track pubertal status and focused on the effects of pubertal timing on social relationships and behavior problems as a way to test whether pubertal changes led to selection or recruitment into different social roles and peer groups. The expectation was that asynchrony with their peers exacerbates the inherent stresses of pubertal transition for early and later matures. Indeed, it appears that early or late pubertal transition pushes some vulnerable individuals toward behavior problems.

Subsequent studies confirmed that view and have gone on to show that maturational timing is a modulator of typical stress during this period of transitions. Both hyper- and hypoactivity and reactivity of the HPA axis are associated with problem behaviors in adolescence that range from disruptive behavior and aggression to alcohol abuse. These problems may have neuroendocrine bases. Recent findings by Susman and colleagues demonstrate interactions between pubertal timing and reactivity in relation to problem behavior in boys, but not girls: later-maturing boys with high cortisol reactivity have increased antisocial and rule-breaking behavior. Another arm of the stress response system showed a different pattern of response. This arm is known as the sympathetic–adrenal–medullary (SAM) system and involves direct neural release of catecholamines into the bloodstream by another region of the adrenal, the medulla. A marker of SAM activity, salivary amylase, showed a different pattern: low SAM reactivity in early-maturing boys was related to rule-breaking and conduct disorder symptoms. The distinct central pathways regulating the HPA and SAM systems permit nuanced responses to stressors in which the two arms operate partly independently and partly synergistically. Clearly, maturation of these two systems during adolescence, their respective roles in meeting the stressors endemic to that period, and their interactions with reproductive maturation are important areas for future investigation.

Understanding the effects of maturational cuing that are mediated by hormones therefore is not simply a matter of their effects on physical-maturational status but also of how maturation of other neuroendocrine systems interacts with the new challenges and opportunities encountered in adolescence. Social Mediation

Many aspects of behavior change in adolescence are shaped by forces independent of hormones. Adolescence radically transforms the social landscape and field of action. Established relationships must be recast and many new ones formed. The importance and content of familial, peer, and other extramural relationships shift. New, more diverse, and more complex and demanding settings are to be explored and claimed. Social networks are to be negotiated, expanded, and remodeled. Figuring out how to behave, identifying social niches and life aspirations, and successfully navigating among all these dimensions of everyday life are major tasks of adolescence. Putting together real-world complexities with the neuroendocrine and morphological dynamics reviewed earlier makes it clear why adolescence appears to be a stressful period. Gendered dimensions of all these tasks also create differences in demands, expectations, options, and opportunities that shape developmental trajectories and color the adolescent experience with gendered rewards and stressors. Indeed, gender differences in susceptibility to stress may be related in part to differences in the types of social stress that are encountered. A survey of the myriad developmental tasks of adolescence should not obscure the important point that adolescents show extraordinary resilience in meeting all these challenges. Those few who fare poorly merit close attention, but the great majority who do well suggest that adolescents could provide an excellent model for understanding resilience, including its endocrine correlates.

Then, too, adolescent behavior problems may be in the eye of the beholder. Adults, whether parents, teachers, or law makers, have expectations and views on social norms that may not be shared, and indeed may be challenged, by the adolescent who is just growing into them. Indeed, many parents find parenting an adolescent stressful, particularly if the adolescent is of the same sex or in the midst of self-formation (individuation), or the parent is divorced or less invested in work or marriage. Often, parent–adolescent conflict and adolescent adjustment problems occur against a background of previous adversity or family difficulty.

Unsurprisingly, there are neuroendocrine dimensions to these linkages. The role of neuroendocrine functioning is
to support the successful pursuit of individual goals such as survival, mating, or belonging, while meeting ongoing demands and vicissitudes of daily life. The evidence reviewed previously outlines some of the many pathways by which neuroendocrine systems build upon experience for adaptive development to meet these roles. Social relationships and conditions are the most decisive determinants of adaptive demands and challenges, as well as the opportunities and resources to meet them. The importance of early caregiving and adversity on psychological and neuroendocrine responsivity to stressors has already been reviewed. Social relationships and quality of life circumstances continue to be important for shaping the course of adolescent development. But the hormone–social behavior interactions may run both ways: previously formed patterns of social cognition and related neuroendocrine profiles may drive the course of social relationships in adolescence, while social experiences in adolescence may shape neuroendocrine development in this sensitive period. For example, established individual patterns of HPA activity appear to influence the quality of relationships girls form during adolescence. Diminished HPA activity reflected in low basal cortisol is associated with poor-quality social relationships with parents, siblings, or peers for adolescent girls, but not for boys. Contrastingly, the established association between testosterone and behavior in boys depends on the social context of their closest peers. High levels of testosterone in boys whose peers ranked as positive social influences are associated with leadership qualities reflected in socially assertive and dominant behaviors. But high testosterone levels in boys whose peers ranked as behaviorally deviant (rule breaking, substance use) are associated with nonaggressive symptoms of conduct disorder.

### Translation to Adolescent Mental Health: The Case of Depression

Worldwide, depression ranks among the top ten sources of lifetime morbidity, a burden that underscores the importance of tracing the genesis of depression to guide efforts at prevention. Rates of depression begin to escalate during adolescence. One of the most outstanding phenomena in developmental epidemiology of western populations is the transition from gender equivalence in rates of depression during childhood to a female preponderance that emerges around age 13. The coincidence with mid-puberty has suggested a role for HPG maturation. And indeed, pubertal increases in both estradiol and testosterone have been associated with risk for depression in girls, with each having independent and additive effects in which testosterone exerts the greater impact.

Depression is also a stress-related disorder: onset is commonly associated with exposure to adversity and depression is associated with altered HPA activity. Thus, the accumulating evidence for increasing levels of cortisol and gender-specific changes in HPA reactivity during puberty has suggested that these changes may play a role in gender-differentiated vulnerabilities to psychopathology, including depression. Accordingly, girls, but not boys, who exhibit greater HPA responses to stress, also report more depressive symptoms.

But the story is more complex and has developmental roots extending back to gestation. Stress during gestation and early childhood influence vulnerability to challenge by shaping the development of reactivity to experience and HPA regulation, as reviewed previously. But these cognitive and neuroendocrine effects are grounded in epigenetic and gene–environment interactions that establish functional characteristics of the neuroregulatory systems that govern experiential processing, appraisal, and thus reactivity. From genetic epidemiology, depression has appeared to be a genetic disorder, showing 37% familial heritability. But the other 63% is related to individual-specific environmental effects. A new generation of research on interactions between environment and genetic polymorphisms for molecules involved in neuroendocrine regulation and on the impact of early environment on gene expression has begun to illuminate the biological bases of those environmental effects.

This work has dealt a final blow to old nature–nurture, gene–environment distinctions and deterministic accounts in favor of nuanced contextualized views of biobehavioral development. A well-studied example of gene–environment interaction involves polymorphisms in the regulation of a key modulator of neurotransmission (the serotonin transporter gene) that influence reactivity to stress and hence alter the risk for depression. These findings are exciting because they point to sites for translation into social conditions over which humans may have some control. Epigenetics, on the other hand, involve variation not in genes, but in the expression of genes. A cascade of environmentally sensitive mechanisms imprint each person’s genetic code with molecules that determine whether and how that genetic information will be read. A powerful example concerns the impact of parental care on the child’s HPA function through epigenetic programming of glucocorticoid receptor expression. For instance, the epigenetic signature has been found whereby childhood abuse alters HPA stress responses and risk for suicide by altering the regulation of glucocorticoid receptor expression in the hippocampus.

### Conclusions

The study of hormones and behavior in adolescence has yielded useful lessons. They include, first, that hormones do not ‘cause’ behaviors. Rather, hormone-behavior dynamics are only to be understood in the contexts of prior developmental events and an interactive biosocial network of which such dynamics form a part. Second, early experiences are formative, particularly for stress reactivity systems. Many associations of hormones and behavior at adolescence are activational, based on organizational effects of these same hormones on target tissues such as the developing brain earlier in life. We now know, however, that a wave of brain development occurs during adolescence and opens a window of sensitivity to organizational effects of hormones at that time. Conversely, adolescent behavior, including psychosocial reactivity to environmental stressors, can also drive hormonal profiles. Third, although reproductive maturation is a signal feature of puberty and adolescence, neuroendocrine systems that handle stressors and stress are also crucial to psychobehavior maturation in this period. Issues of stress, adaptation, and resilience are central to adolescence. Fourth is the insight that biological
systems are designed to capture information from the environment of which social contexts are defining features. Hormones play a central mediating role by reflecting regulatory mechanisms influenced by prior experience and by orchestrating the allocation of the body's material and cognitive resources to meet demands in view of ongoing priorities. Specific mechanisms involving gene–environment interactions and epigenetics are known to mediate the interface of person and context, often via modulation of neuroendocrine activity. Fifth, greater insight into hormone–behavior interactions provides insight into the sources, as well as prevention and treatment, of adolescent mental health problems such as depression. In sum, hormone-behavior dynamics reflect the inherent interdependence of body, mind, and context in human development.

Global Perspectives

This discussion of hormones and behavior offers insights but has limitations worth considering in view of conditions among contemporary global youth. Virtually all research represented in this article draws upon studies conducted in western settings that represent but a small fraction of humanity. Some evidence-based theories of development and hormone–behavior interactions at adolescence may hold across the range of human cultural, ecological, and economic-political diversity, but that is an empirical question for future science to address. Many more lessons likely will be learned in the process. Meanwhile, consider the challenges for global youth in view of our knowledge about lifetime interactions of social context, experience, and neuroendocrine development in the formation of hormone–behavior interactions in adolescence. Globalization and urbanization have refashioned the conditions of childcare by transforming family formation, parental wage labor involvement, and daily life patterns. Concomitantly, worldwide efforts for universal schooling have transformed childhood and adolescence: in 2002, youth worldwide spent on average 10.5 years in school. These global shifts also have opened up media, mobility, and economic landscapes for adolescents and youth. Nevertheless, nearly half of adolescents have grown up and live in poverty, and 15% of youth ages 15–24 are undernourished and 15% are unemployed.

Evidence in the aforementioned reviews shows that factors ranging from gestational stress and low birthweight, to early caregiving, adversity, and uncertainty in childhood and adolescence, and family, peer, and other extrafamilial adolescent relationships all shape neuroendocrine and behavior development before and during adolescence. Global trends touch on each one of these factors. Developmental science is just beginning to explore the biosocial pathways of resilience and risk by which adolescents negotiate a rapidly shifting world of uncertainty, opportunity, and adversity.

See also: Brain Development; Genetics; Transitions into Adolescence.

Further Reading


