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Lisa Wright and Stan Kutcher
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Adolescent Brain Development

Lisa Wright and Stan Kutcher
Dalhousie University

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ABSTRACT

Adolescent brain development is a fascinating, newly developing field that has so much to offer almost anyone interested in learning more. Adolescence has only come to be established as a unique developmental phase in the last few decades or so. We now know that the human brain undergoes dramatic developmental changes in the postnatal period, not only early after birth but also extending all the way into adulthood. These changes are not uniform, in that the brain regions undergoing the most change during adolescence are not the same as the regions that changed most in the early life period, and the processes of change also differ as we age. Some of the most important changes that we see during the adolescent period are: 1) pruning (or removal) of excessive neural connections, 2) increases in white matter, the portion of brain matter that allows different regions to communicate with one another, and 3) thinning of the cortex, which is comprised of the outer layers of brain matter. Compared with other areas of the brain, the frontal and temporal cortices undergo the most protracted changes in their structure, implying that developments in these areas play a large role in providing the foundation for adolescent behavioural changes. In this book, we compare adolescent behavioural changes with ongoing changes in the brain and discuss potential implications for health and educational policy-making.

KEYWORDS

adolescence, brain development, teen brain, prefrontal cortex, frontal cortex, temporal cortex, protracted brain development, neural pruning, white matter, cortical thinning, health policy, education policy.

Contents

CHAPTER 1

Introduction

Do you recall how you felt and behaved during the days of your youth? What was it like to leave childhood behind and become a teenager? How did your life and you change across the teen years, and when do you think you finally reached adulthood? Some of us may say age 18, while others may say not until 35.

Many of us have fond memories of the adolescent period as a time to explore life's possibilities, have fun with friends, and not worry too much about the future. For some adolescents, however, due to life circumstances such as living in poverty, being exposed to persistent violence, or experiencing major negative life challenges (such as the death of a parent), this time in life may not hold so many fond memories as it does for others. However, even given such negative circumstances, adults will often joke and laugh about the trouble they caused or experienced as a teen, even though it may have been no laughing matter at the time. Yet, it often seems that social norms expect teens never to be in or cause trouble. Maybe, however, causing or experiencing trouble as a teen is actually a typical, normative part of adolescent development.

The term "trouble" is subjective and there is a big difference between the types of impact "trouble" can have. Selling an illegal drug, getting home very late at night, drinking too much, drinking and then driving, failing an examination, cheating on an examination, wearing sandals to a funeral or shorts to school in winter, bullying someone, or stealing a car (etc.) are all examples of things that can cause "trouble" for a teen. However, the examples surely are not the same—or, could they be more alike than we think? Could all these "troubles" be different types and degrees of expression of the same brain developmental processes that we consider to create the defining characteristics of this period in life? And, if that could be the case, what other impacts could these brain changes have? For example, could they also be the foundation of the innovation, exploration, idealism, creativity, and energy that teens are known for? Here we will explore those possibilities.

Our main objectives for this book are two-fold: first, we'll examine how behavior, emotions, and cognition typically change during the adolescent period and also what we know about developmental processes going on in the brain at this time that may be the foundations underlying those changes; second, we'll try to understand what makes some individuals vulnerable to a negative developmental outcome, while other individuals are resilient or flourish in similar environments.

A better understanding of what factors may lead to positive life outcomes may go a long way in efforts to develop better interventions and treatment strategies for adolescents experiencing social, emotional, and behavioral difficulties, or who have developed a mental disorder. Perhaps this understanding may also foster the creation of healthier families and communities. Thus, it goes without saying that this is an exciting endeavor!

1.1 OVERVIEW

The overall goal of this book is to provide a description of what is currently known about adolescent development, in terms of changes in emotions, cognition, and behavior, as well as related changes in the brain. How does what we now know about the way people's brains grow and develop during adolescence explain what we refer to as the psychology of adolescence? However, before we attempt this task we need to keep two important caveats in mind.

First, what we know about the adolescent brain is still very much limited by the nature of the tools we have to study it, the sophistication of the research methods we have used, and the length of time we have been studying it. Thus, as science and technology develop and our research capabilities improve, our information about how the teen brain develops may change, and we may end up discarding what we consider to be good explanations in favor of better or different explanations. Therefore, we should refrain from getting too confident that we know all that we need to know about the teen brain! Indeed, we expect that perhaps in ten years a part of what we today think is correct will turn out to be incorrect. Unfortunately, we don't know which part that will be!

Second, while there may be strong correlations between certain brain changes and the emergence of different kinds and degrees of teen behaviors, that does not mean that those changes directly lead to those behaviors, nor does it mean that those changes necessarily lead to those behaviors. We are aware that co-relation does not equal causality and also that ongoing environmental influences on how teens' brains grow and develop may have substantial impacts on their emotions, cognitions, and behaviors. Simply put, the circumstances of adolescence may have strong impacts on the development of adolescents.

Therefore, we start this exploration of adolescent psychology, not with certainty but with humility and the willingness to change what we think is correct as the scientific evidence develops over time. In conjunction with our scientific training and expertise, we also carry with us the awareness that cultural knowledge (or indigenous or traditional knowledge) also provides different useful information that is very important to consider in gaining a big-picture perspective.

Many of us may not really be comfortable in our knowledge of what the word "psychology" means, even though we may use it on a regular basis. In the sciences, psychology is most commonly defined as the study of behavior and/or mental states and processes. Notice the euphemistic "and/or" conjunction here, which seems to denote that studying either behavior OR mental states and processes should be classified under the general umbrella term of "psychology." Many colleagues in university departments of psychology would argue that, at its core, psychology is the study of behavior, and it must always relate primarily to behavior. They may argue that the measurable output of our mental processes is the effect that it has on behavior, an effect that can be observed and quantified and studied directly. From a clinical perspective, this approach holds a degree of promise; it provides normative behavioral data to doctors and other healthcare workers and can help us develop predictive models of future behaviors. It thus allows us to develop a better understanding of environmental factors involved in generating certain behavioral outcomes. This then can help us better determine what kinds of interventions may be helpful in increasing the probability of better health outcomes. One important consequence of this kind of reasoning has been the recognition that interventions for children who are exhibiting behavioral difficulties that begin early in life and use specific types of environmental manipulations may be more effective than either interventions beginning later in life or different types of interventions. Both timing and type of intervention may each play an important role in levels of effectiveness.

Despite these merits and well-demonstrated impacts, this idea that psychology is simply the study of behavior leaves some burning questions.

(1) What goes on INSIDE the mind—just because we can't see it with our eyes doesn't mean processes aren't going on INSIDE our brains. What is going on in there when we express a behavior?

(2) How do mental processes relate to ongoing behavior? Why are only SOME mental processes predictive of a change in behavior, whereas other mental processes do not seem to induce an observable behavioral change? Also, for those suffering from psychological problems or mental disorders, the major challenges that they are facing may not be behavioral problems but rather inappropriate, unwanted, and often distressing thoughts and emotions.

Inevitably then, the study of behavior is inextricable from the processes that regulate it. Given the current state of the field of neurobiology, we know that the organ most responsible for regulating behavior is the brain. We have a solid basic understanding of how nerves function in their control of various emotional, cognitive, and behavioral functions, although we are still learning a great deal about many aspects of the brain circuits and systems involved. Thus, we now understand the brain to be both the organ that creates the mind and the place from which our emotions,

cognitions, and behaviors originate. Those who study how brain function relates to behavior or who study brain circuits and processes in their own right are said to be in the field of neuroscience, and these approaches help us better understand the brain in health and in illness and how to intervene to help build healthy brains and help heal those that are not functioning well. Our book is based on this understanding, and it is from this perspective that we approach the topic of adolescent brain development and adolescent psychology. A teenager is not just a bundle of behaviors but a complex organism with complicated and interwoven emotions, cognitions, and behaviors. We need to try and understand all these at the same time.

The overarching theme of our book is that, by attempting to link adolescent brain development with changing adolescent psychology, we may gain important insights about how behavior, emotions, and cognition are all regulated by the brain and about what distinguishes the regulation of adolescent psychology from that of adults or younger children. We will begin with a general consideration of human brain development across the lifespan and of adult brain function. From there, we'll move in Chapter 2 to a more focused look at brain development during the adolescent period. In Chapter 3, we will describe patterns of adolescent psychological changes, and in Chapter 4 we'll take a look at teen social dynamics. In Chapter 5, we will attempt to link these behavioral observations to what is known about ongoing developmental changes in brain function. In the final chapter, Chapter 6, we will consider how our knowledge of adolescent psychology should be applied, in terms of legal, educational, and medical policies and current practice guidelines.

1.2 THE NATURE/NURTURE INTERACTION: GENES, DEVELOPMENT, AND EPIGENETICS

As with so many other books on psychology, development, or the brain and behavior, we must start by considering, in the most basic sense, what makes an individual an individual. Well, okay, sexual intercourse is the usual way in which a new individual is made, but we're not talking sex education here—what we're interested in is: How does the individual grow from the point of conception into a fully formed adult? And, of course, we know that this individual growth and change does not end at adulthood either. Also, what makes some individuals develop differently than others, even if they experience very similar environments? It is these kinds of questions that we will keep in mind here as we briefly review what we currently know about how genes work, how they are regulated over time, and how the environment impacts gene function. Historically, we have spent a long time arguing over the presumed different impacts of genes (called nature) and the environment (called nurture). Today,

most of us realize that this argument has been a colossal waste of time. It is not nature vs. nurture that is the issue here. The argument is actually a question: How do genes and the environment interact to determine the growth and development of an individual? When we are able to answer this question we will have moved forward in our understanding of ourselves and of our species. And, with a bit of luck and lots of hard work, we may be able to learn how to create better outcomes for everyone.

The significance of the nature/nurture dichotomy originates in the historical division of development theorists into two categories: those who believed our genes determine who we become as adults (the nature side of the debate) and those who believed that nothing about our psychology is determined at birth—that we are born as "blank slates" (Latin: *tabula rasa*) and only experience will determine who we become (the nurture side of the debate). Looking back historically we see that many people spent much time, energy, and effort on this topic, including some famous philosophers and university professors! And, we are only too aware of some of the social, economic, and cultural conflicts and chaos that have arisen as a result of these ideas.

With the rapid knowledge we have accumulated over the last few decades we are now comfortable in saying that the "blank slate" theories are wrong, but also that theories that only considered the role of inheritance are also incorrect. Findings of experimental research have shown time and again that the genes we inherit most certainly play an important role in shaping who we are and who we become. Compellingly, results from twin studies, adoption studies, and other family studies all show that the more genetically related two individuals are, the more similar they are in adulthood on a number of physical, emotional, cognitive, and behavioral dimensions, regardless of whether or not they were raised in the same environment [1–4]. For example, identical twins, born with almost the exact same genetic sequences, can be raised apart and they still end up more similar in adulthood than fraternal twins or other sets of full siblings who were raised together. Fraternal twins and other full siblings (same biological mother and father) generally share approximately 50% of the genetic sequence in common. Furthermore, fraternal twins or other full siblings who were raised apart are more similar than adopted siblings who were raised together.

In addition to these family studies, there are other major pieces of evidence for which the "blank slate" theories do not provide useful explanations. Fetuses already start behaving in certain ways even before an individual is born, and there is evidence to suggest that prenatal behavior may be predictive of later behavior. For example, fetal reactivity in the third trimester of a pregnancy (months 6 through 9) is predictive of infant reactivity at six weeks of age [5]. Also, some individuals inherit problematic gene sequences that result in an illness, regardless of what sort of environment the individual is raised in. Examples of relatively simple genetic disorders with this pattern of inheritance include Tay-Sachs disease, hemophilia, and cystic fibrosis.

From all of this evidence and more, we now understand that genes indeed do play a major role in determining who we are and who we become. But, and this is a very important "but," who we are and who we become does not only depend on our genes! It is not only nurture nor only nature.

Indeed, there are clear findings that genes do not play the ONLY role in guiding development—in many different studies, the environmental context has been shown to contribute significantly to developmental outcomes. Genetically identical individuals DO show behavioral, cognitive, and emotional differences in adulthood, and this is attributed mainly to their differential personal experience, although slight variations in some genes may also have an impact, as even with identical twins, no two people have the exact same genetic sequence throughout their genome (e.g., infrequent mutations in the code). As we can see, this is becoming very complicated!

We now know that numerous features of the environment may impact on an individual's development and affect who they are and what they will become. These environmental factors can be substantive and even life threatening (such as living in a war zone or severe and persistent stressors in early childhood, such as neglect or abuse), or they may be subtler (such as whether your mother held you most often on her left or right arm [6])! We also know that some of these influences can start impacting how brains develop while a person is still in the womb, i.e., maternal starvation or malnourishment for the mother (severe life stressor), smoking, or living in poverty (subtler stressors). Just as there can be negative environmental stressors (a neural stressor could be considered anything that impacts the brain from outside the brain, such as sounds, chemicals, touch, social interactions, a drug, etc.) that can impact on how a person's brain develops, there can be other kinds of environmental influences on the brain that lead to positive outcomes, even in the presence of negative stressors (for example, the availability of loving, positive, and reliable adult support for a child exposed to severe stress early in life).

So, time and again, as this evidence accumulates, scientists are led to the conclusion that BOTH genes and environment make significant contributions to the regulation of how development unfolds. Put simply, both genes (nature) and environment (nurture) are important to who we are and who we become. This is a much more complex and nuanced understanding of human development than either of the two competing historically prevenient theories. It also leads us to be wary of simple theories or simple explanations of complex human psychology. And, just to be more complicated, the outcomes of this gene/environment interaction may be different for different people and for when during the life span (for example, in the womb, in the first three years of life, in adolescence, etc.) the environmental impact occurred. A final consideration is that recent research shows that there seem to be a number of different genes (that everybody has) whose purpose seems to be to help us adapt to whatever environmental conditions that we are in. The more we learn

about these genes (and their different varieties, which can be different in different people) the more we are coming to understand that unique combinations of these so-called "adaptability genes" seem to be very important in how different people adapt (whether they show resilience or failure) to the environments that they are in.

Since genes are so important in regulating the process of how we develop (who we are and who we will become), we should briefly review what we know today about genes and how they work. Recognizing that our knowledge is rapidly changing, it is possible that what we think is correct today may turn out to be less correct next year. So now we will recapitulate important lessons of genes and their work, lessons that we have only come to recognize in the last couple of decades.

We'll tackle a few important questions here; namely: (1) Where are our genes? (2) What are they? (3) What do they really do? In answer to our first question, our genes are located in every cell of our bodies—that is, a full set of all of our genes is located in each and every cell of the body (except sperm cells and egg cells, which, through a special cell division process called meiosis, end up with only half a set or one of each pair). This is quite amazing, really, when you think about it. When we were conceived, we were originally only one cell, receiving half of our genes from our mother and the other half from our father. The genes in that one cell had all the information needed to create us, a multicellular entity with cells that have unique and special functions that all work in concert (though not always harmoniously) with each other. The genes in that one cell gave rise to our brains, our hearts, our fingers, our bones, our eyes, and everything else we are. And, wherever in the world we live, that same genetic mechanism works the same way. It does not matter if you are in Brunei, Bangladesh, Brighton, or Boston—you have a heart, a stomach, a kidney, and a brain. And as you grew from that one cell, over time, regardless of where you are at certain times in your development, you are the same. So at 5 months in the womb or at 3 years of age or at age 15, your different body parts are similar—everywhere in the world.

Although we have an abundance of different kinds of cells making up our bodies, they generally all have a central compartment called the nucleus, and this is where the genes are stored, in tightly wound bundles called chromosomes. Humans have 23 pairs of chromosomes, whereas other species have different numbers. Not everything in a chromosome is a gene however! We will come back to that later.

With respect to our second question above, well, really our genes are nothing more than strings of chemicals called nucleotide bases joined end to end. These are the components of what we call the DNA. The nucleotide bases act as the characters of the genetic code, like the 26 letters of the English alphabet. The DNA is structured in the now famous and well-known "double helix" format. This genetic code, however, is made up of only four characters and instead of forming

legible words it forms gene sequences that can be "read" by tiny biological molecules that gain access to the stands of DNA. These molecules, which are made up of proteins found in the cell, "translate" the code—essentially, they use it as a blueprint in the production of new protein molecules. The characters are known as A, C, T, and G. These abbreviations stand for adenine, cysteine, tyrosine, and guanine, the four nucleotide bases present in DNA. An example of the way that we represent a gene sequence would be:

AATGAAAAAGCAGATTTTTTTATTATGATGTTTCTCCATATTTGGCATTG.

This particular combination is the first part of a real gene, the NR3C1 gene [7], which provides the code to make glucocorticoid receptors, protein molecules that play an important role in the body's response to stressors, as well as a number of other functions. Some genes have allelic variants, meaning that particular sites within the gene sequence vary among individuals. That means that while everyone has the same gene, different people can have different varieties of that gene. For example, think of bread as a gene and its alleles as its varieties (rye, whole wheat, bran, etc.). And, just like the varieties of bread can give us different tastes, the varieties in the genes can modify how that gene works.

The issue is complicated, however, by the fact that the DNA packaged in the nucleus of each cell is not single-stranded; it is actually double-stranded. The example sequence from the NR3C1 gene is the sequence found on only one of the strands, called the positive (coding) strand or sense strand. The other side, called the negative or antisense strand, is lined up alongside the sense strand and joined to it at every one of the nucleotide bases, with G bases always joined to C bases, and A bases always joined to T bases (Figure 1). The sequence of the antisense strand that would pair up alongside the sense strand shown above would read:

TTACTTTTTCGTCTAAAAAAATAATACTACAAAGAGGTATAAACCGTAAC.

To tackle our third question about genes—"What do they really do?"—the double-stranded structure has to be taken into consideration, as do some other aspects of the way the DNA is packaged in cell nuclei. As we can see, this is becoming pretty complicated already, and we are not yet even close to finishing this explanation.

Remember that we said that genes are actually a code, each consisting of a readable sequence of nucleotide base pairs that can range anywhere from 500–500,000 or more nucleotides in length. These readable segments of DNA are interspersed amongst long sections that are not part of the genes, called untranslated regions. Some people call this "junk DNA." Not so long ago

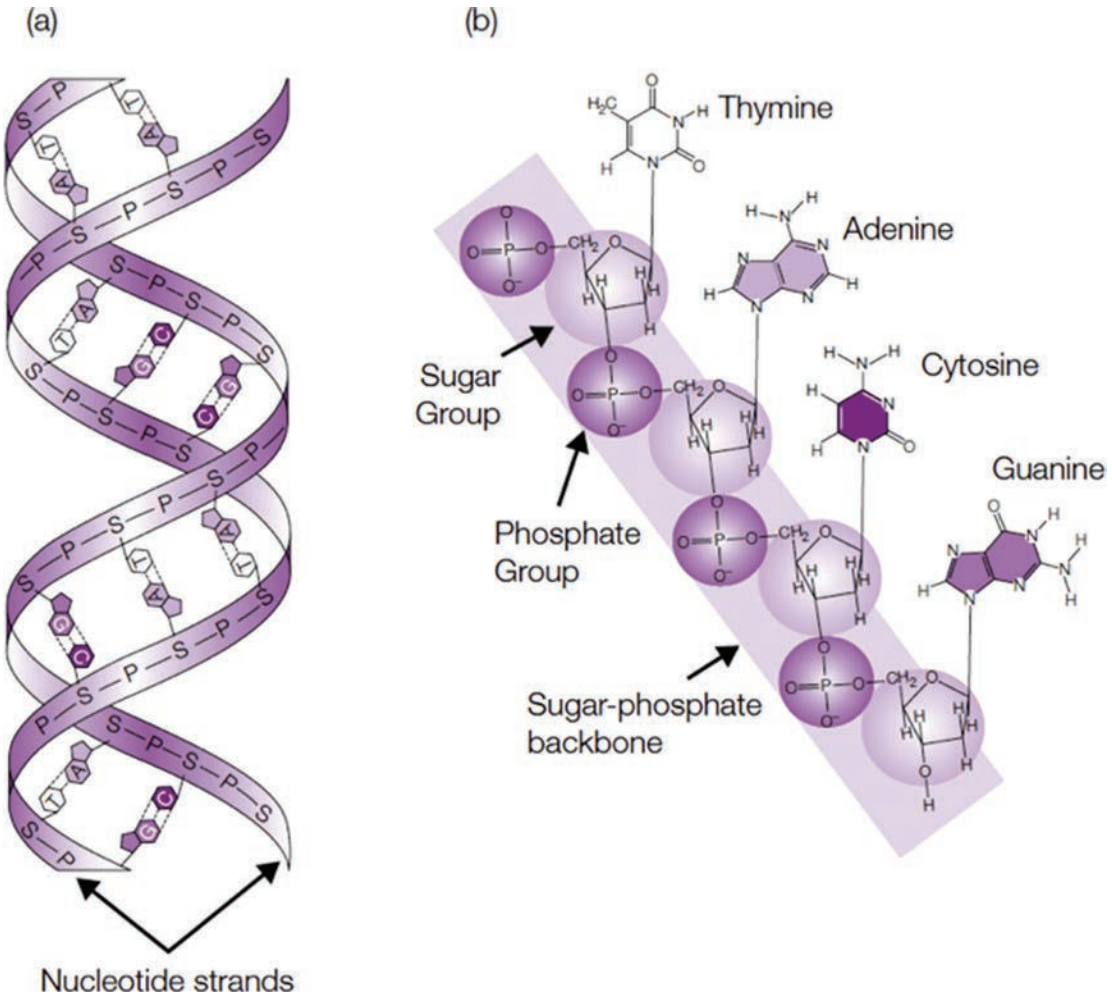

FIGURE 1: (a) A representation of the structure of DNA showing how the sense strand is joined to the antisense strand by chemical bonds between the nucleotide bases of each strand (S—sugar group, P—phosphate group, A—adenine, T—thymine). (b) Detailed structure of the four nucleotide bases in DNA showing how they form bonds with the sugar-phosphate backbone. Reprinted with permission from M.H. Johnson [17].

we thought that this DNA was not important, but recently we are learning that we may have been too hasty in that conclusion. What exactly that "junk" does we are not sure, but maybe it's not junk after all.

In general, each gene encodes instructions for the production of a certain protein molecule, such as the glucocorticoid receptor protein encoded by the NR3C1 gene. Everything our bodies are made up of and all of the processes that go on within them involve protein molecules; thus, there is a huge number of different protein molecules encoded for within the genes. It's the proteins that do all the hard work making things such as brains, hearts, and lungs! They also maintain the ongoing functions of these organs over time.

Each gene has a "start" spot near the beginning of its sequence, and these start positions, called promoter regions, attract biological molecules that attach to the DNA and carry out the actual "reading" of the DNA code. Once the biological machinery attaches to a promoter site, the gene is said to be turned "on" and construction of the protein that the gene codes for is initiated through a series of steps that we will not go into here, except to say that they ultimately represent what is called "gene expression"—the *in vivo* production of proteins. Often, many copies of a protein molecule will be made at a time, while the gene is turned "on," and the proteins act in conjunction with other proteins in the body in dynamic, complex ways to carry out different kinds of biological activity. So, the complexity increases. It's not as simple as the protein is made and off to work it goes! What and how it works may be impacted by how much is made and who its co-workers (other proteins it interacts with) are.

Notice that DNA is not read from start to finish. Only particular segments are meaningful, and even in these meaningful bits some segments will need to be used more often than other segments. This is because the body needs more of some proteins than others. How does the body decide which genes to turn on, when, and how much expression should occur before the gene is turned back off? It is this area of genetics that researchers are currently struggling to study and understand, and it is very complex. Perhaps even more complex than all we have already discovered.

However, this is very important. Understanding the factors that regulate gene expression is key to understanding the nature/nurture interaction, because we now know that many environmental factors regulate gene expression. For example, referring again to the example of the NR3C1 gene, if an individual is in an environment filled with many stressors, they will require a different level of expression of this gene than someone who is not living in such stressful circumstances. This of course is one of the untapped mysteries of the brain, but it helps us understand just how well suited the brain is to adapting to the environment that it is in. After all, that is perhaps its most important function: helping us adapt to our environments, so that our species will continue over time. Of course, we also create our environments to a large degree, so it is hard to escape the conclusion that we are likely to become what we have previously done.

Putting this into a big-picture context, consider two hypothetical individuals who are not related. They would have different allelic variants of the same genes at many sites within their genome, and these differences in their gene sequences would be responsible for some of the differences in phenotype (how they look, behave, and think) between the two individuals. However, the two individuals would also show different levels of gene expression of all the genes they have in common (as well as the genes that vary), and this is regulated on an ongoing basis according to both internal and external cues, cues that would be different for the two individuals based on their personal experiences. Thus, the environment actually plays a constant role in regulating gene expression, and many of the behavioral, emotional, or cognitive (taken together as psychological) differences between the two individuals are attributable more to their varying levels of gene expression than to their specific DNA base pair sequence (i.e., *how* they are using their genes, not what specific allelic coding sequence they possess). Studying such regulation of gene expression by environmental factors is the task of researchers in the newly emerging field of epigenetics. ("Epi" means "over" or "above" in Greek and is intended to represent a top-down regulation over gene expression in this context—regulation that involves limiting or opening up accessibility of the genes to the biological machinery that will read the code, whereas traditional genetics relates more to individual differences in the sequence of the code.) So, the complexity continues. And to make it even more complicated, many different genes are involved in the creation, maintenance, and modulation of the multiple neural circuits that make up each of these complex brain functions. By the way, did we mention that these circuits are all linked to each other, and that activities in one can impact activities in many others? More on that later.

In essence, the emergence of the field of epigenetics represents the inevitable marriage of nature to nurture. It is not, as we have said above, nature vs. nurture. It is understanding how nature and nurture work together to make us who we are and who we will become. And remember, the environments that we live in (nurture) are often shaped by or chosen by us—so the interaction is not one way! Our environments change us, and we change our environments, and on it goes over time. Acceptance that nature and nurture are inextricably linked has been one of the more important theoretical milestones in our understanding of our species and us. It will be crucial to apply this understanding to our study of adolescent brain development as our knowledge about how this interplay works itself out continues to grow.

1.3 PHYSICAL DEVELOPMENT

In this section, we'll review the basics of what is known about human development, in terms of the timeline of physical development from conception to maturity. Although this book is about the

adolescent brain, it is not possible to separate the brain from the body. The brain acts on the body (for example: through the hormone signals that begin the onset of puberty; through the peripheral nervous system that sends signals directly from the brain to all parts of the body) and the body acts on the brain (the oxygen and glucose needed to drive this amazing organ are delivered through what the body does).

1.3.1 Prenatal Growth

The first step in human development happens at conception (Figure 2), which occurs through the joining of an egg cell and a sperm cell, usually by means of engaging in sexual intercourse. Typically, an egg is released about once a month in an alternating fashion from one of the two female ovaries and moves down the corresponding fallopian tube toward the uterus, a process called ovulation. If intercourse occurs around the time of ovulation, a sperm cell may find and penetrate the egg, thereby fertilizing it.

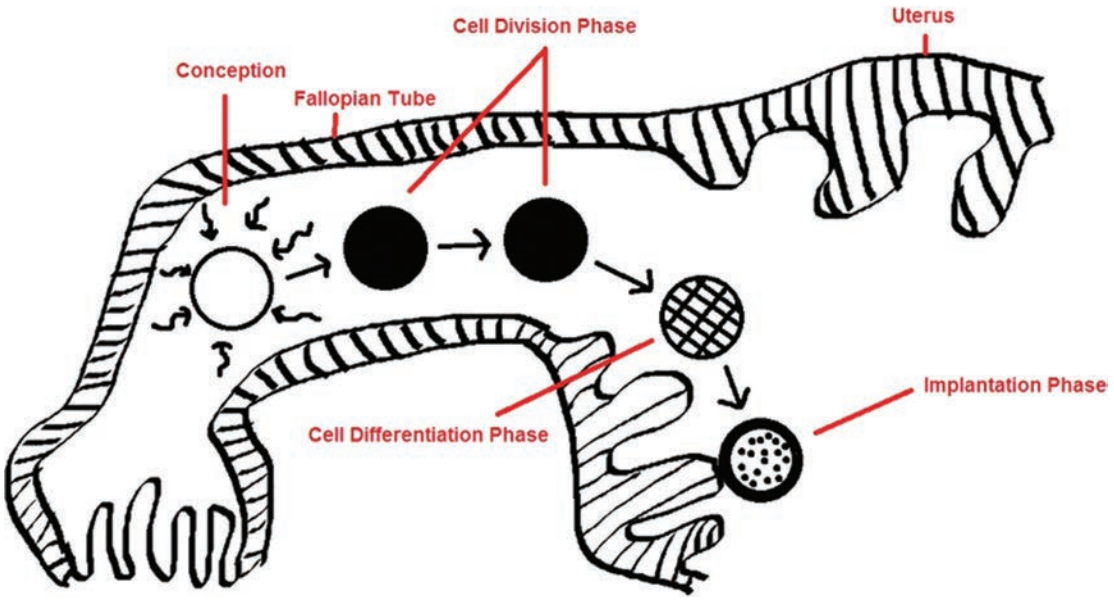

FIGURE 2: A Schematic representation of human conception and the early events that follow. Adapted from D. Boyd and H. Bee [8]. The authors acknowledge assistance from Ms. Kate Elliot in producing this figure.

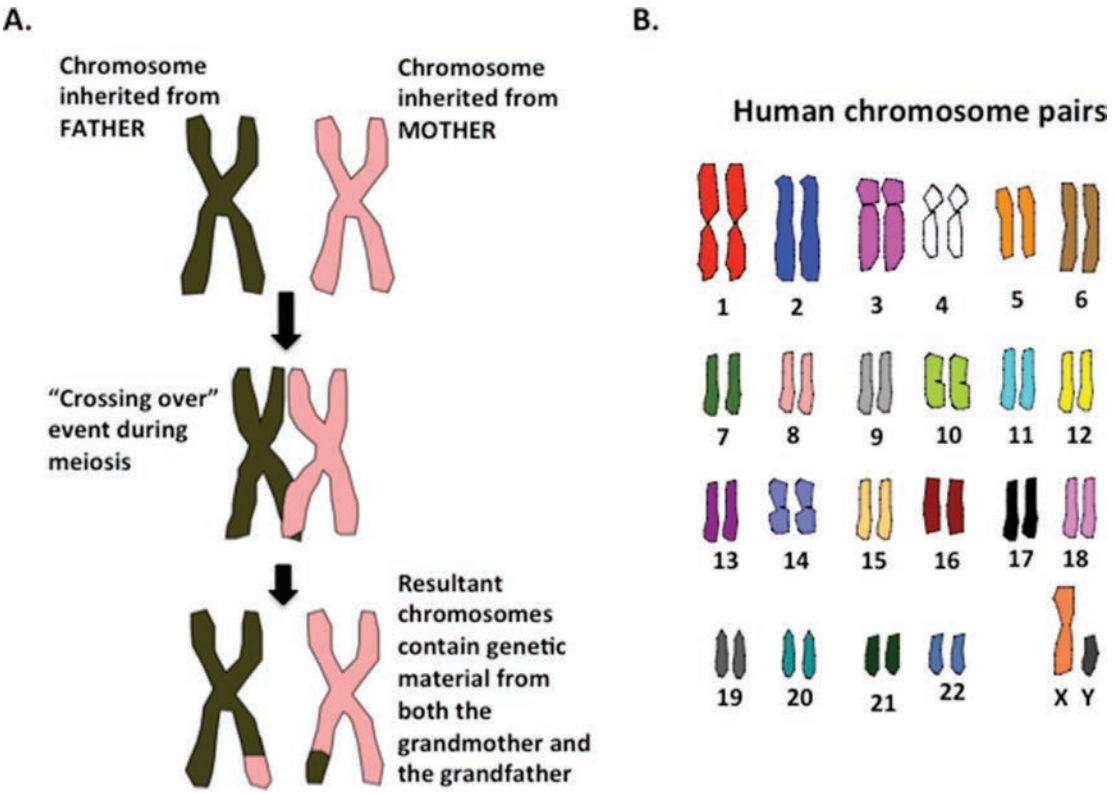

FIGURE 3: (a) A schematic representation of a "crossing over" event occurring during cell meiosis. Assuming this individual is female, each resultant chromosome comprises the genetic material for one egg cell. Each of the two egg cells would contain genetic material from both the mother and the father of the individual in a unique combination! The same would be true if the individual was male, except the resultant two chromosomes would comprise genetic material for two sperm cells. (b) A representation of the 23 chromosome pairs in the human genome. Original drawing by L. Wright.

Each egg and sperm cell has a single set of 23 chromosomes contained within, and these combine together to form a brand new, complete set of 23 pairs of chromosomes with a totally original package of DNA with its own combination of genes and allelic variants. In addition to the new random pairings of chromosomes, a complex process called "crossing over" that occurs during meiosis ensures that the single chromosome set contributed by each of the egg and sperm cell is made up of an entirely unique gene sequence. In other words, each chromosome isn't simply passed down "as is" from either one grandparent or the other, but rather, each chromosome inherited from either parent will contain a combination of the genetic sequences of his or her own parents (Figure 3a).

Essentially, there is much ado about introducing genetic variation into each new generation. Nature rolls its dice, and you never know for sure what you're going to get!

The sex of the individual is inherited via the sex chromosomes, one of the 23 pairs of chromosomes in human cells. The sex chromosomes are the only pair that can be made up of two different types of chromosome, X and Y chromosomes, whereas each of the other pairs has two copies of a single type that are numbered Chromosome 1 up to Chromosome 22 (Figure 3b). If the sperm cell contributes a Y chromosome, then the individual will be male. If the sperm cell contributes an X chromosome, on the other hand, the individual will be female. The egg cell will always contribute an X chromosome, because, women, who make the eggs, have two X chromosomes for their sex chromosome pair. Thus, when making eggs, women only have the option of contributing an X chromosome to the single set of chromosomes that will be contained in each, whereas males have an X chromosome and a Y chromosome for their sex chromosome pair and can therefore contribute either type of sex chromosome to each sperm cell during sperm production.

The fertilization process results in a zygote, a single cell with a full set of genes, which subsequently multiplies into all the myriad cell types that make up the human body. Once in a while, the zygote duplicates itself into two separate individuals that become identical twins. However, most twins are the result of two separate eggs being fertilized by two separate sperm cells, which produces a set of fraternal twins (approximately 2/3 of all twins [8]). Due in part to the use of fertility treatments in the western world, approximately 3% of births here result in more than one baby, most of which are twins [9].

As the single-celled zygote begins to multiply, it also moves from the location of fertilization down the fallopian tube to the uterus. By the time it reaches the uterine wall (~3–5 days), it is called a blastocyst and has begun to subdivide into an inner and an outer layer of cells. The outer layer facilitates implantation into the uterine wall; the inner layer becomes the embryo.

Implantation is usually complete by the second week after conception. After this, the embryo begins to form the rudimentary basis for all of its organs, and, following six weeks of growth, the basis for all of the organ systems is in place [8]. At this point, approximately two months into pregnancy, the embryo becomes a fetus.

The following seven months of pregnancy is called the fetal stage and involves further development, growth, and refinements of all of the organ systems (Table 1). The fetus starts off weighing only about a ¼ oz and measuring 1 inch in length, but by birth the new baby weighs on average about 7 lb and measures 20 inches in length. When born, unless there are birth-related complications, the baby's organs are all fully developed. All except for the brain, that is. Much of the brain's growth happens after birth. That is why young children's heads grow so much faster than the rest of them. Figure 4 shows the progression of prenatal brain development.

TABLE 1: Milestones of the Fetal Stage

PERIOD	WHAT DEVELOPS
Weeks 9–12	Fingerprints; grasping reflex; facial expressions; swallowing and rhythmic "breathing" of amniotic fluid; urination; genitalia appear; alternating periods of physical activity and rest
Weeks 13–16	Hair follicles; responses to mother's voice and loud noises; 8–10 inches long; weighs 6 ounces
Weeks 17–20	Fetal movements felt by mother; heartbeat detectable with stethoscope; lanugo (hair) covers body; eyes respond to light introduced into the womb; eyebrows; fingernails; 12 inches long
Weeks 21–24	Vernix (oily substance) protects skin; lungs produce surfactant (vital to respiratory function); viability becomes possible, although most born now do not survive
Weeks 25–28	Recognition of mother's voice; regular periods of rest and activity; 14–15 inches long; weighs 2 pounds; good chance of survival if born now
Weeks 29–32	Very rapid growth; antibodies acquired from mother; fat deposited under skin; 16–17 inches long; weighs 4 pounds; excellent chance of survival if delivered now
Weeks 33–36	Movement to head-down position for birth; lungs mature; 18 inches long; weighs 5–6 pounds; virtually 100% chance of survival if delivered
Weeks 37+	Full-term status; 19–21 inches long; weighs 6–9 pounds

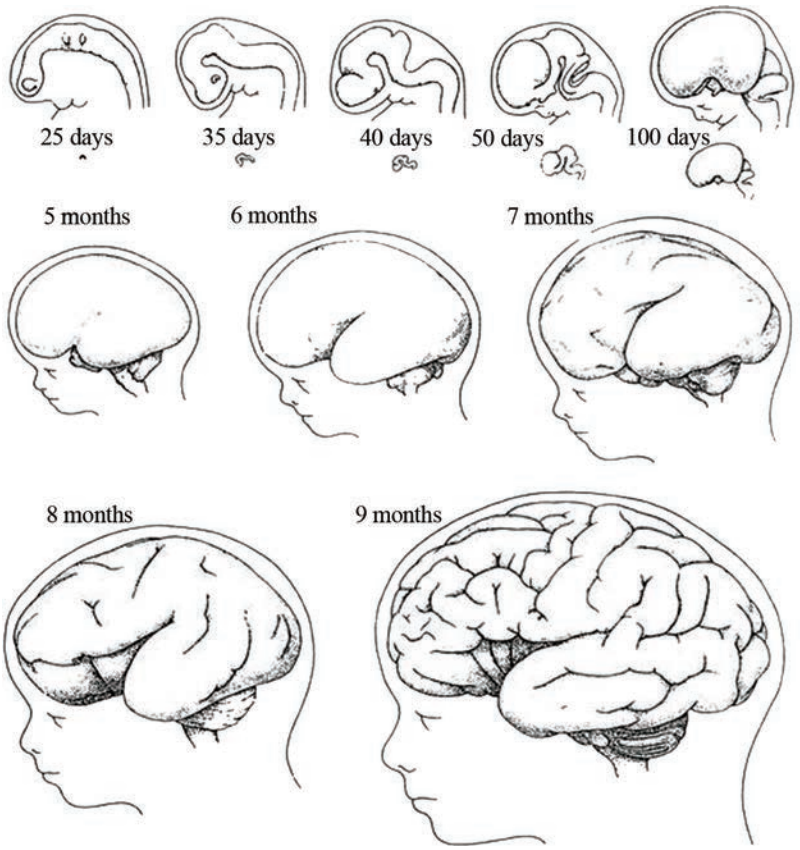

FIGURE 4: Pictorial representation of prenatal development of the human brain. The small images underneath the labels 25 days, 35 days, 40 days, 50 days, and 100 days show the brain development at the same size scale as the images in the row below. Reprinted with permission from M.H. Johnson [17].

1.3.2 Postnatal Growth

The early childhood period is characterized by rapid physical growth. In the first year of life, a baby usually adds approximately 10–12 inches to his/her birth height and triples his/her birth weight [8]. By age two, the baby has become a toddler and is approximately half as tall as he/she will be in adulthood [8]! Growth slows down somewhat at this age, and the individual begins to add only about 2–6 inches in height and 6 pounds per year for the remainder of childhood.

There are also some notable changes in body composition and proportion that occur across childhood and adolescence. The head of a newborn baby is proportionately very large relative to

his/her body as a whole; however, the head becomes proportionately smaller across development, as it undergoes much less growth than the body core and extremities after the first few years of life. In terms of body composition, the major changes involve fat, muscle, and bone.

The subcutaneous fat layer peaks at approximately 9 months of age and then declines until the early school years (6–7 years of age), at which point it begins to increase again. For girls, the proportion of body weight made up of fat continues to increase across the adolescent period, and the proportion made up of muscle decreases, whereas the pattern observed in boys is just the opposite. This results in a clear sex difference in body composition by adulthood. During adolescence, there is a marked "strength spurt" in both boys and girls, but especially in boys, and this results in a large sex difference in adult strength as well (see [10]).

Also, the composition of muscle itself, as well as that of bone, changes across development. Both the muscles and bones of an infant have a high water content, relative to those of an adult. The water ratio of muscle decreases at a steady rate throughout childhood. Similarly, bones undergo a steady process of hardening as they age, and they are not considered fully ossified until after puberty. The skull bone and bones of the hand, wrist, ankle, and foot are not fully formed at birth. At birth, the skull is made up of a number of separate pieces that later fuse into a single bone [8]. The spaces, called fontanels, allow the head to be compressed slightly during childbirth without injury to the brain. The fontanels may also play a similar protective role during the early childhood period, in the event of falls or other accidents involving the head. The fontanels have usually closed over by 12–18 months of age, once the individual has gained an increased capacity for self-protection from head injury. The hands, wrists, ankles, and feet, in contrast, develop additional bones after birth, and these become increasingly articulated across development; also, this process occurs slightly earlier in girls than in boys, constituting another sex difference.

Puberty, although a hallmark of adolescence, is not synonymous with it. Some people think of the two terms as signifying the same thing, but reaching puberty means that someone is going through the changes necessary to become capable of reproduction, whereas reaching adolescence denotes a period of transition from childhood to adulthood. Puberty, therefore, involves biochemical, physiological, and behavioral changes. It usually marks the beginning part of adolescence. Adolescence, on the other hand, involves not only pubertal changes, but also cognitive, emotional, and social changes, many of which are described throughout this book.

Many, if not all, of the changes of puberty are guided by massive hormone changes in the body's neuroendocrine system. The gonads (testes in males; ovaries in females) become functional endocrine (hormone) organs through the establishment of the hypothalamic-pituitary-gonadal (HPG) axis. The HPG axis is the brain-body system that allows the brain to regulate the production and secretion of gonadal (or sex) hormones, such as estrogen, progesterone, and testosterone. Once

in the bloodstream, the gonadal hormones are distributed throughout the body and act on various different steroid receptors located in organs and tissues. Activation of these receptors modulates a variety of bodily processes and also creates negative feedback loops within the HPG axis itself.

Although the hormone cascades of puberty are complex and beyond the scope of this book, they have been studied for several decades and are fairly well understood. The initiation of the HPG axis is jumpstarted by a change in the release pattern of luteinizing hormone (LH) from the pituitary gland. Specifically, LH begins to be released in a pulsatile fashion at this time, and this initiates the cascade of other changes.

The timing of these changes is not fully understood, although it is thought to involve two major factors: (1) changes in the sensitivity of the HPG axis's negative feedback loop and (2) changes in the brain's opioid system and its modulation of the neurosecretory cells of the pituitary gland, where LH is made and released. Interestingly, as the pituitary first starts to release LH in a pulsatile fashion, it happens only during the nighttime before becoming pulsatile all the time, suggesting an important connection to the sleep-wake cycle. The timing of puberty can also be influenced significantly by a number of different environmental, experiential, or lifestyle factors, most importantly weight/eating habits and stress, indicating that the pubertal process is programmed to be somewhat flexible with respect to timing.

While this section is meant to provide a broad overview of physical development, a more detailed coverage of pubertal and adolescent physical development can be found in Chapter 5 of "Stress and the Developing Brain" [10].

1.4 BRAIN DEVELOPMENT

Now that we've had a chance to review human physical development generally, we'll focus on brain development specifically and consider how it fits into the overall developmental timeline. It is assumed that you, the reader, have a basic understanding of the general principles of how nerve cells communicate. These principles can be reviewed in some detail in Chapter 2 of "Stress and the Developing Brain" [10]. Basically, brain neurons communicate with each other through the release of chemicals called neurotransmitters into small spaces (synapses) between neurons. Neurons are arranged in networks or circuits that act in concert with other circuits to initiate and control all brain functions. Other kinds of cells in the brain, such as glial cells, support neuron activity and have other functions as well, including production of the myelin sheaths that wrap around neuron projections called axons and assist them in their functioning. This section will provide an overview of human brain development. This will set up a framework for studying the changes that occur during adolescence.

As mentioned previously, the foundation for all of the organ systems of a newly developing individual, including the nervous system, is already in place two months after conception, when the embryo becomes a fetus. Some of the cells of the developing embryo will by now have differentiated into neurons, the specialized cells that will go on to develop into brain matter. From about two and a half to five months into the pregnancy, there is a rapid burst of cell division that generates new neurons, a process known as neuronal proliferation. Interestingly, the vast majority of neurons that make up the brain are all formed by cell division in two particular regions (proliferative zones), called the ventricular zone and the subventricular zone. The cell bodies of the neurons that make up the adult brain have all been created by approximately seven months *in utero* (excluding a relatively small number of neurons that will be made later on in particular brain regions that are capable of creating new cells later in life, a process known as adult neurogenesis).

Following neuronal proliferation, the neurons must then move to the specific part of the brain where they will reside in the fully developed individual, and they do not reach anatomical maturity until this process, called neuronal migration, is complete. That is to say, it is not until a neuron reaches its final destination that it sprouts an axon and dendrites, the anatomical structures that allow neurons to communicate with one another (Figure 5). The process by which neurons communicate involves the generation of synapses—points of near contact between two neurons, through which information can travel using chemical neurotransmission.

Interestingly, the brain overproduces neurons during the prenatal period and then scales back the number that it keeps for the adult brain. It does this through a process of programmed cell death called apoptosis, whereby some neurons are marked to be degraded in a controlled fashion. This procedure begins before birth but continues on into postnatal life and is now understood to be an important aspect of child development, particularly regarding its role in shaping neural networks that involve the complex circuits within the cerebral cortex [11], the part of the brain most associated with human-specific attributes. Furthermore, the concept of human brains developing more than what is necessary and then scaling back to keep only what is needed in adulthood seems to be a biological strategy that applies also to other aspects of brain development as well. For example, the number of communication points between neurons and the number of neuronal receptors (locations that receive chemical messages) both undergo a similar pruning process during development, especially in adolescence.

Synapses begin to form among neurons after they have been created and have migrated to their destinations in the brain. We call this process synaptogenesis. Also, specialized glial cells begin to wrap sheaths of myelin, a fatty, insulating substance, around the axons of neurons in a process called myelination, which increases the speed at which messages can be sent along neurons. Synaptogenesis and myelination begin in the womb, are both highly active around the time of birth and in early life,

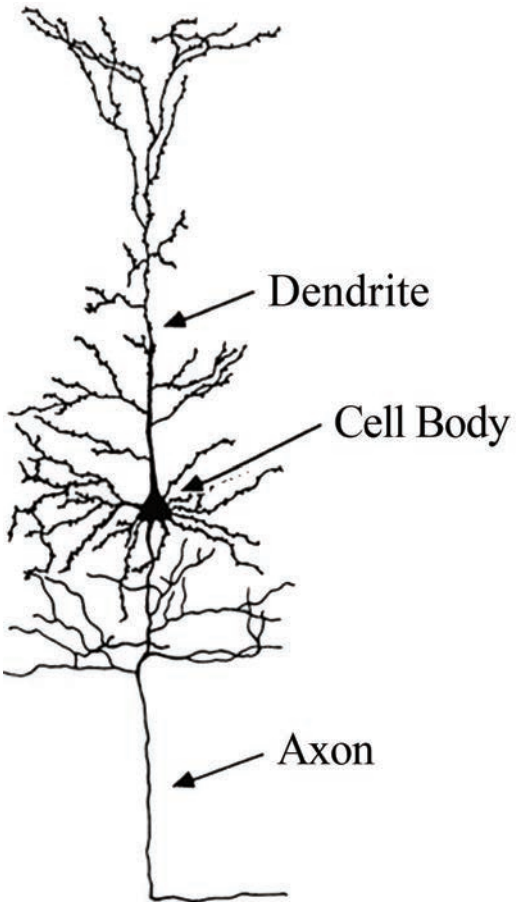

FIGURE 5: Pictorial representation of a mature neuron showing its dendrites and axon. Reprinted with permission from M.H. Johnson [17].

and then each taper off at some later point. Myelination is thought to extend into the adolescent period, and it is during this time that nerve cells develop their maximum message velocities. As for synaptogenesis, it begins with neurons sprouting a great number of dendrites that initially contact many other cells, but, over time, through the process of synaptic pruning, many of these connections are then removed, leaving relatively stable neural circuits that underpin all brain activities.

At the time of birth, the brain exhibits a very high degree of plasticity, meaning that it has the capacity to achieve a number of different possible developments that will impact on how it functions. This is accomplished in numerous different manners, including neurogenesis and synaptogenesis.