MOOD

The Key to Understanding Ourselves and Others

Patrick M. Burke

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Inquiries should be addressed to
Prometheus Books
59 John Glenn Drive
Amherst, New York 14228-2119
VOICE: 716-691-0133
FAX: 716-691-0137
WWW.PROMETHEUSBOOKS.COM

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This book is dedicated to my late wife, Velma Dobson, PhD,
the single greatest and enduring influence in my life,
for showing us how to live a life of integrity
and in the end how to die with grace and dignity;
and to our children, Meg and Andrew,
and to the newest additions to our family, Tiffany Gromlich and little Oliver.
I am forever grateful for their willingness to help; their expertise;
and their unquestioning love, support, and encouragement.

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ACKNOWLEDGMENTS

This book is the fulfillment of a promise made to my wife, Velma Dobson, before she passed away from complications of Amyotrophic Lateral Sclerosis (ALS, or Lou Gehrig's disease) in April 2010. I had started out to write a book about psychiatric disorders in youth for the nonexpert, but a radically different book emerged as we grappled with her disease, and I began to better understand the role mood plays in our lives and how the forces that act on mood could serve as a unifying theme for the book and help us surmount the challenges of ALS.

The original impetus for a book grew out of the frustration I experienced as a child psychiatrist as changes in healthcare delivery increasingly limited my time with children and families to brief assessments and medication management with little room for any but the most formulaic explanations and answers to questions. There was in addition an underlying dissatisfaction with the standard approach of discrete disorders with overlapping risk factors and treatments that put the disorder and not the person at the center.

The solution came when, stimulated by a lectures series by Richard Solomon,[1] I realized that Martin Heidegger's ideas on mood could provide the needed theme. The approach and ideas for this book were initially developed and tried out at La Frontera, Inc., in Tucson, Arizona, and I am especially thankful to the staff and patients of the center. When my wife became homebound, I stayed home to help. We worked in parallel—she continuing to work with her research colleagues in an incredible display of courage and perseverance, while I researched background material and worked on a book proposal. The book was written after she died, informed by a now-deeper understanding of the role of mood and the connections between mood, relationships, commitment, and action.

Many people have helped me along the way to writing this book. I most gratefully acknowledge two individuals who played seminal roles in my career. The late Sean Lavelle, MD, a professor in my medical school in Galway, Ireland, saw something in a bored medical student who told him he really wanted to

study developmental psychology. He started me on a path that led to Lewis P. Lipsitt, PhD, who graciously took me on and persevered with me as his graduate student at Brown University. This was one of the great adventures of my life, an exciting time when I was exposed to investigators and graduate students, among them my future wife, full of ideas and doing cutting-edge research.

My psychiatric education followed at the University of Washington under the tutelage especially of David Raskin, MD, and David Rowlette, MD, and where Charles Nagel, MD, advised me that the key to difficult psychiatric problems was to "find the affect," an adage that has been with me since. And where Eric Trupin, PhD, and Robert Reichler, MD, taught me the value and necessity of an empirical and multidisciplinary approach to child psychiatry.

Throughout the process of writing this book many friends and colleagues listened patiently to my musings, helping me think out ideas, providing insights, confirming the value of my approach, and in many cases providing helpful comments on various drafts of proposals and chapters. I particularly want to thank Anne Libecap; Linda Karl, MD; Helen Herziger; Clara Billotte; Kelly Vogiatis; Caroline Duffield; and Richard Hinton, PhD. I am also grateful to the child psychiatry fellows (especially Adolfo Martinez, MD, and Anna Shier, DO), residents, and students in the Child and Adolescent Psychiatry program at the University of Arizona for their patience with my lectures and supervision, insightful comments, and encouragement.

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CHAPTER 1
OVERVIEW

We are told that nothing in the world is certain except death and taxes. But we can add a third certainty. We are always in a mood. What is more, we are constantly faced with references to mood: popular tunes of happiness or sadness; pundits opining that the economic mood of the country will determine the outcome of an election or that the mood in the locker room will determine which team wins the game; advertisements telling us a product will change our mood and our lives. Mood is everywhere and somehow is linked to what we find important and meaningful. Emerson described life as a train of moods strung like beads, which, as we pass through them, prescribe what we see.[1] For the poet W. B. Yeats, literature is wrought about a mood or a community of moods.[2]

But our moods change, and we seem to have little control over when and how the change occurs. It seems we can neither command nor will our mood to change. Rather, our mood changes, and it is only after the change that we realize we are in a different mood. Most of the time, we pay little attention to changes in our mood or how the changes occur. But the change can be disturbing. We find we are sad, anxious, uneasy, or feel threatened. If the new mood interferes with our ability to function, the change may amount to a mood disorder. For many, these disorders can be destructive to their lives and can warrant professional attention. How does this happen?

We have good reason to suspect that difficulties with mood originate in developmental events. Changeable moods are accepted as part of childhood and adolescence. Take, for example, the irritable colicky infant, the temper-prone toddler and preschooler, or the moody adolescent. There is abundant evidence that most psychiatric disorders among adults that involve significant changes in mood first become evident in youth. At a clinical level, the annual rate of depression in adolescents is estimated to be 5–9 percent, and in prepubertal children the rate is estimated to be 1–2.5 percent.[3] Between 2–5 percent of youth are diagnosed with an anxiety disorder.[4]

How do these disorders come about? And what can be done about them? Perhaps the most common view is that dysfunction in brain chemicals is the underlying issue. Stress is implicated, whether due to conflicts or loss in relationships, or other life events. Genetic influences are also thought to play a role, and much research is geared toward understanding how genes and environments interact to produce disorders. Similarly, research in personality development shows the importance of individual temperament. Advances in the neurosciences have implicated brain circuits and other bodily systems, and these are also subject to genetic and environmental influence. Moreover, there has been massive growth in pharmacological treatments, as well as in psychosocial treatments each with its own school of thought and practitioners. Complicating matters further, diagnosis and treatment, especially in youth, have become controversial issues. Advances in all these areas have been rapid and have originated from a range of disciplines. As a result, the available information is widely distributed in literature and is so complex that, unless you have some expertise in the field, the general reader is likely to have difficulty integrating the findings.

Beyond questions of causation and techniques to remedy problem behavior, how do mood and the disorders involving mood fit with how we see ourselves as agents in the world? Are we passive and simply subject to our genes and our environments? What role do we play or can we play? Can mood be linked to responsibility? Is there a way to address these questions and unify the above themes to guide the nonexpert?

Despite the breadth and depth of current studies, surprisingly little attention has been paid to the subject of mood itself and mood disorder. Most often, the focus is on emotion and mood is simply subsumed, used interchangeably with emotion, or is subordinated to cognitive activities. This book takes a unique approach by treating mood as a central controlling factor that from childhood becomes the basis upon which we choose and act, and sets the stage for how we are throughout life. The basic idea is that mood connects the person and the world, and this connection is built and shaped over the course of development. How might this work? If we think of mood as a phase of the activity of neural circuits and bodily systems that continually process information about the world, then the feelings of mood and the associated bodily systems provide the mechanism for the connection. They enable the assessment of possibilities and become the basis for action.

Development comes into the picture because genetic and environmental influences starting with the fetus create the underlying systems. The stress response system, which is active when destabilizing events occur, is especially relevant because it has profound influence on developing neural circuits. How this system functions influences the degree to which someone is vulnerable or resilient when something challenging happens. Disorders involving changes in mood emerge as breakdowns in the connections occur, and resilience comes from the connections being able to surmount challenge.

The book is organized as one possible roadmap that ties together the many biological and social factors that not only shape development and functioning but also underlie the emergence of disorders and are key to prevention and treatment. There are four key themes set around two core notions, the importance of the individual and the importance of developmental processes.

The central theme is that mood reflects the way we are tuned into the world, reveals our possible options in a particular situation, and thereby becomes the basis of action. The basic idea derives from Martin Heidegger, primarily his major work *Being and Time*.[5] Although Heidegger did not write about children, we have adopted some of his central insights and placed them within a developmental context. The first theme is nested in a second theme—we are self-constituting. If we consider the self as a way of being, then who we are as agents is realized only by what we do and by what we make of ourselves as we live an active life.[6] Relationships with others are at the core of these processes. Complex interactions between the child, other people, and the world underlie the child's struggles with becoming autonomous and responsible for himself. Mood, by revealing our possibilities, plays a fundamental role in development because development is the step-by-step process of becoming self-constituting. Interactions with others and the world have mood at their core, and they reciprocally are at the core of how mood develops and can be changed.

To illustrate this approach, imagine a child as a stringed musical instrument with its combinations of strings and sounds. The tuning—mood—of the instrument at any given moment is how the child tunes into the world. But the child is a constantly resonating living organism. Therefore, a mood is always present and since a child has many strings and combinations of strings, many moods are waiting to emerge. From the earliest beginning, genetic and environmental influences form the strings, and throughout life continue to influence the strings. The tuning underlies how events appear to a child, rather than being a reaction to an event or how the child thinks about things. When something happens, the child's strings reverberate and the resulting mood depends on the tuning of the individual string. The child's tuning (mood) alerts him to the possibilities present, paving the way for him to choose and act.

Chapter 2 examines mood and what mood does and attempts to differentiate mood from emotion. Heidegger argues that we are not detached beings, observing and making decisions based on what we see and then acting accordingly. Instead, we always already find ourselves in situations that matter to us and that typically involve others around us.[7] Things matter to us because each of us is uniquely disposed or attuned to the world. Our attunement reveals the world to us, and our attunement is mood. He elaborates that what and how we experience is a function of our involvements with things, and especially our involvement with others. Relationships and situations present possibilities, and our tuning differentially disposes us to the possibilities presented. As we interact with the world, our senses provide information. Moods (how you are tuned to the world) also provide information and reveal the situation. They tell us what matters and has significance.[8]

Think of yourself as a very nervous and fearful person, who is walking alone down a darkened street. Certain features, like doorways and shadows, stand out. Your mood (fearfulness) alerts you to possible danger and provides the conditions for you to react with fear (an emotion) should something happen. Mood is like a special sense that not only tells you about your world (the world is frightening, this situation is positive) but also informs you about yourself—you are a happy person, or a fearful person, or you are nervous and not doing well.

But we are not in full control of our situations. The range of possibilities presented to us is limited, and we vary in skill and understanding on how to proceed. This brings us to Heidegger's ideas about fundamental moods and his concept of authenticity,[9] or what is unique and particular to each individual.[10] For the most part, we live life to suit or to meet the expectations of others by following our social and cultural roles and avoid any underlying anxiety about our being. But when critical events occur that bring us face to face with our finite being, the submerged anxiety reveals the fragility of the way we live, and we're faced with making choices. To become authentic we need to act on this realization, becoming responsible for ourselves and choosing our own way to live.[11]

How might tuning develop? Mood is present from the beginning, well before speech and language develop. Parents describe their newborns as "happy," "content," and "fussy" or as "hard or easy to console." They often say their child "was born" that way. Chapter 3 traces the development of key moods and related emotions (sadness, guilt, anger, fear), emphasizing the role interpersonal relationships play. The chapter introduces temperament, a key construct that is partly defined in terms of characteristic moods and forms the building blocks of

personality. Later chapters discuss the relation of temperament and personality to the emergence of anxiety, depression, and disruptive antisocial behavior.

The third theme is that mood and tuning arise through the activity of certain neural networks[12] and body systems.[13] The underlying concept is that the body is a framework through which we perceive the world, and the possibilities offered by the world.[14] *Imagine a six-month-old infant lying on the floor and playing with small blocks. The infant grasps a block, stares intently at it, puts in her mouth, exchanges it in a fumbling way for another, drops one, and searches until she picks up another block, which again goes in the mouth while her small hand manipulates it. This infant is experiencing the world of blocks through her bodily senses—touch, sight, and taste. She is forming some rudimentary sense of the possibilities of the blocks, and in so doing of her world.*

Chapter 4 discusses how the nervous system analyzes and evaluates information about the world, enabling and coordinating our reactions and responses by organizing the activity of neural networks involved in mood and emotion.[15] How these networks are made, and how they function, sets the tuning of each child. We can think of the circuits as the strings of the instrument. Assuming the brain's networks function normally, the child will be appropriately happy; sad; or in an average, everyday mood. But if the tuning of certain string(s) is off, then the world may appear scary or highly exciting, and moods may be intense, subdued, or labile as those strings are sounded.

The way a child is tuned emerges over the course of development as genetic (chapter 5) and environmental influences (chapters 5 and 6) combine to form the circuits (the strings of the instrument) and set how they function in daily life and under conditions of stress. Individual differences in behavior reflect functional differentiation within the circuits.[16] The stress response (chapter 6) is a complex array of neurohormonal processes that is activated when a potentially destabilizing event occurs.[17] A variety of genetic and environmental influences affect the stress response, and interactions and relationships with others are crucial influences that are essential for its normal development. How this system responds plays a large part in the development of the personal characteristics associated with resilience and vulnerability.

Not all children who experience stressful events (e.g., parental separation and/or change in schools) become depressed or anxious, nor do all children in a family with familial or genetic risk factors (a depressed or alcoholic parent) develop a disorder. There is a wide range of responses to the environment. Some children (and adults) respond positively and effectively, but others respond in negative and/or

ineffective ways. Someone who responds well in one type of situation may not do as well in another. Why do some but not all children at risk develop a disorder? How can we relate how a child is tuned over the course of development to factors such as genes, stress, and the environment involved in mood disorders? Individual differences are key to understanding what happens.[18] Chapter 6 introduces some current models that are helpful in explaining how multiple influences (genetics, early experience, temperament and other characteristics of the child, relationships with others) may interact to leave some individuals vulnerable and others resilient.[19] The models can also be the basis of prevention and treatment efforts suggesting both targets and strategies for intervention.

The fourth theme is that disorders emerge out of the interaction of events and the functional status of neural circuits and systems. When vulnerable children are faced with stressful events, significant alterations may occur in mood, behavior, and biological functions. Particular patterns of dysfunction underlie the principal disorders in youth that are characterized by mood disturbances: anxiety, depression, bipolar disorder, and antisocial/oppositional disorders. Such features tend to cluster, and the clusters are the basis of the diagnostic categories. The diagnostic system is currently in transition. Chapter 7 sketches some key background issues to the diagnostic process and outlines key changes in the new manual.

Chapters 8–10 consider the main disorders that involve mood and mood changes. Although the focus is on youth, the relevance to adults is indicated throughout. In each case, the mood and emotion component is explored along with neural circuitry and the stress response to illustrate from a developmental perspective how the disorders come about and manifest and why they often occur together. It will be seen that in each case, the disorders have typical mood and emotion profiles, physiological changes, and action patterns. They also show substantial overlap; the stress response system has a role in each; and relationships play central roles both by influencing the development of mood and the circuits underlying mood, and by the role they play in precipitating disorders. In each case current research on neural circuits and the stress response are explored, and shows common patterns of activity in circuits related to mood and emotion. Anxiety (chapter 8) is characterized by worry and fear and is concerned with present or future threats of harm. Anxiety disorders reflect dysfunction in circuits underlying fear, manifest the physiological changes reflecting flight or fight, and action is typically avoidant. Sadness and negative thinking characterize depression. Depressive disorders (chapter 9) are concerned with loss, reflect dysfunction in neural circuits involved in mood, manifest physiological changes reflecting altered stress responses, and diminished activity. Bipolar disorder (chapter 10) involves mania and depression. Elated or irritable mood and grandiose thinking characterize mania. It can be viewed as a dysfunction of neural systems underlying reward. The stress system plays a role, and activity levels are increased. This disorder is increasingly and controversially diagnosed in children and adolescents. The background to the controversy is explored, and proposed changes are discussed.

In terms of mood, antisocial and disruptive behavior presents some interesting and challenging issues. Typically, disruptive and antisocial behavior is viewed as not being related to mood but as defiance of authority, rule breaking, disregard of the rights of others, and with aggressive behavior as a characteristic action. However, it is increasingly clear that mood plays a very importance role in antisocial behavior. Chapter 11 addresses the important roles irritability and indifferent mood play, as well as the role of a diminished as opposed to an exaggerated stress response. In contrast to other disorders, it will be seen that a key subset of antisocial youth and adults show a different pattern of dysfunction in mood-related circuits from the other mood-related disorders.

Prevention and treatment approaches are discussed in chapter 12. We evaluate key elements of the most prominent current procedures, examining their stance in light of the themes of the book. What is their approach to mood? How do they deal with relationships with others? What are the effective ingredients? To what extent do they guide the child and family in discovering what matters and in choosing among available options in ways that foster autonomy and learning to take responsibility for one's life?

In addition to psychotherapeutic techniques, a variety of medications are in use (chapter 13), and they are increasingly combined with psychosocial treatments. Medication therapy is discussed in relation to its affect on tuning of the neural circuits and related systems.

Chapter 14 considers medical illness, the diagnosis of which can present significant challenges to affected youth and families. Medical illness can also serve as a model situation to illustrate the application of ideas expressed in this book. Many illnesses present significant burdens for both child and family, as well as the loss of options and the need to reorganize and refocus. Circuits involved in mood regulate the stress response, and these circuits are also involved in the immune response and inflammation. While most children and families surmount the challenges, many illnesses are associated with increased rates of anxiety, depression, and other disruptive behavior.

CHAPTER 2

WHAT DOES MOOD DO?

The central theme of this book is that mood is a central controlling fact that reflects the way we're tuned in the world and how it becomes t basis of choice and action by revealing our possible options in a particu situation. Because of this, mood plays a fundamental role throughout develc ment and in what we become as persons. This chapter explores some of the id behind these assertions. The basic ideas derive from Heidegger, primarily l book *Being and Time*,[1] but his approach to mood is also seen in a second work which he provides a lengthy discussion of boredom.[2] Because Heidegger is no riously difficult, we also draw on various commentators who have helped clar his ideas. Matthew Ratcliffe, in particular, critiques and further elaborates Heidegger's ideas about mood, and so a number of Ratcliffe's ideas are incorp rated.[3] To develop the themes, we must first explore issues in terminology. T point is to draw broad distinctions between *mood* and *emotion*, as it will beco clear that a settled definition of either term is not available. A key point will that mood can be thought of as the basis for emotion.

We freely use the terms *mood*, *feeling*, and *emotion* in everyday conver tion and generally seem to communicate what we mean when we use them. E once we start examining these words, we run into difficulty, and distinguishi them turns out to be a challenge. The first difficulty is that each one cover wide range of experience. Consider the following: *She said she had been sad weeks*; *He had the feeling something was wrong*; *I feel I have lost my way*; *He ha school*; *You could tell by her behavior how angry she was*; *I was in such a bad mo I'm so scared. My heart is pounding, my hands are sweaty*; *She said she felt num He felt tired*; *He felt a sharp pain*; *Her mood was infectious*; *The mood of the cro made him feel uneasy*; *The mood of the voters will determine who wins the electi* Which of these statements represent a mood? Most readers will readily ident some as moods. But some will be identified as feelings; others as emotions; so may be difficult to place, and some may fit all three definitions.

Affect is another term widely used, especially in psychiatry. The mental status examination distinguishes between mood and affect. Moreover, older versions of the *Diagnostic and Statistical Manual* (*DSM*) classified mood disorders as affective disorders. The *DSM-IV-TR*[4] defines mood as an emotional climate: a pervasive and sustained emotion that colors the perception of the world. Affect, on the other hand, is described as the more fluctuating changes in emotional weather. Neither the glossary nor the index has an entry for *emotion*.

So what is mood, and how does mood differentiate from feeling or emotion? We first address feeling and then discuss differences between mood and emotion. All experiences involve sensation, like what is included in the phrase "I feel."[5] There are also multiple uses of the word *feelings*, ranging from the feeling of an itch to feeling sad.[6] We also sense what it is like to experience something. If we pick up an object, we feel that object and the movements we make. According to Laura Sizer, feeling is a phenomenally conscious sensation, a state that one occupies as opposed to an action one performs. This definition not only captures the sensation of an itch or of feeling cold; it also captures "the way things are with you now," the importance of which you will see when we discuss mood.[7] We now see a wide range of experiences that constitute feelings, some of which are moods and others emotions. How can they be distinguished?

WHAT IS MOOD?

According to *Merriam-Webster's Collegiate Dictionary*, mood is a "conscious state of mind or predominant emotion"; a "receptive state of mind predisposing to action"; or a "distinctive atmosphere or context."[8] The *Oxford Companion to Philosophy* says that moods are "states of mind of an emotional cast which are temporary, yet which color a person's responses and reactions quite generally," and whose "focus is on a pattern of behavior manifesting a current state of mind, and not on the intended consequences of the behavior."[9] These definitions indicate that moods are forms of feelings, but while they highlight certain characteristics of mood, the definitions do not fully distinguish mood from emotion.

People are always surprised when it is pointed out that we are always in a mood. But we cannot be in an alert state without being in a mood of some kind. Mood is a property of consciousness that seems to set the tone or flavor of conscious states.[10] You could even argue that moods are present during sleep. We commonly have anxiety-laden dreams and wake up feeling as if we didn't sleep well. Could it be that the child who wakes up grumpy in the morning was in an irritable mood during sleep, and the grumpiness is, in part, a continuation of the mood? Or do we always wake up in a neutral or even a mood-less state, if only for a fraction of a second before a mood then appears?

People are frequently surprised to learn that moods arise outside of awareness. But if you pause to think about it, a mood is already present by the time we become aware of any mood change. We don't have full control over the mood we're in, and we can't easily change our mood. We may not be able to change our mood without taking some action.

Interestingly, while we say we have moods or feelings, we typically say we are in a mood, but we do not say we "mood." Mood, it seems, is something we are in and not something we do. Mood is not an action. Moods monopolize and characterize the total "set" of a person while he or she is in a mood.[11] Emerson said that "life is a train of moods like a string of beads" that "paint the world their own hue," adding that each mood "shows only what lies in its focus."[12] A sad child or person tends to experience everything in a negative light. There is evidence to support this, as mood has broad effects on attention and memory.[13] For example, negative moods narrow attention and focus, while positive moods have the opposite effect.

An interesting characteristic of mood is that a mood may be public and contagious. For example, a room full of people (or a crowd) may exhibit a particular kind of mood. *Members of a large crowd celebrating a team victory may all be in a happy mood; someone who happened by could note the mood of the room and could easily get caught up in that mood.*

Moods can be short-lived or long-lasting. But particular moods or a tendency toward particular moods can be characteristic of an individual. Here mood is a component of temperament (chapters 3 and 4).

If a mood is always present and we can't change it on demand, what are moods about? Moods are not about some particular thing but rather are unintentional (*intentionality* is a philosophical term referring to how "one's subjective state relates one to the world"[14]). One view is that moods relate to everything and capture the whole world as their focus.[15] Ratcliffe suggests that feelings are about how we relate to the world and to the sense that we belong to the world, and moods are in this category.[16] We feel attached to somebody or to some place; we feel bored, we feel alive, we feel connected, we feel lost, and so on. *John always feels uneasy; John was sad and did not know why; John awoke feeling happy.*

WHAT IS EMOTION?

The historical interest in emotion goes back to the ancient Greeks.[17] But despite intense interest from philosophers, psychologists, and neuroscientists, we still have no single accepted definition of emotion.[18] While there is agreement on what counts as emotion (hate, fear, jealousy, or grief), there is less agreement on what an emotion is. *Merriam-Webster's Collegiate Dictionary* defines *emotion* as "the affective aspect of consciousness"; a "state of feeling"; a "conscious mental reaction subjectively experienced as strong feeling"; and "usually directed toward a specific object."[19] In this instance, emotion—like mood—is described as a feeling, but thinking about something and forming judgments are added components. An example from the developmental psychology literature suggests that emotion is "the process of registering the significance of a physical or mental event as the individual construes significance."[20] *Eight-grader John becomes angry and rushes at Tom because of comments Tom made about John's mother.*

Note that, in contrast to mood, we don't say that we are in an emotion, but we do say we emote. Emotions do not just happen but rather tend to be reactions to something. *John was angry because he was given extra homework.* An emotion seems to be something we do,[21] and an emotion has physiological components that reflect the bodily systems involved in processing information and in preparing to or responding to an event. One prominent expert defines emotion as a distinct, integrated, physiological response system, and lists four components: (1) a prototypical form of expression (e.g., facial expression), (2) consistent autonomic changes (e.g., changes in heart rate), (3) a distinct subjective state of feeling, and (4) a characteristic form of adaptive behavior.[22] *When John heard the comments about his mother, he felt his breathing change, his teeth clenched, and his heart raced as he rushed at Tom.*

Emotions typically do not last long, and most subside as soon as the triggering or provoking issue is resolved. *John's anger evaporated when his teacher relented and gave less homework.* Moreover, emotions do not seem to color the entire situation the person is in. *John may say he hates his teacher, but this does not extend to others or to other situations.* Being public is also not readily seen as a property of emotion. *John's friend Mary might witness John's anger over a homework assignment, but Mary would not easily become angry unless John convinces her that the homework is unfair and should be protested.*

Ratcliffe identified feelings about how we are in or attached to the world as existential feelings, and among these are feelings commonly identified as moods.[23] In contrast, he identifies feelings that are directed toward things in the world as emotions: they relate to something specific. *John is angry with Tim; John ran from the room in fear when he saw the dog.* However, we will use *mood(s)* since that is the term referred to in both general and clinical use, and doing so will avoid confusion when discussing clinical disorders.

HEIDEGGER AND MOOD

Heidegger suggested that we always already find ourselves in situations where we are always engaged in practical concerns or projects that matter to us and that offer certain, but not all, possibilities as we plan ahead and look to the future.[24] Crucially, we never view the world as if we were outside looking in or as if we are distant from things in the world where we have a vantage point to understand the world, but instead we experience ourselves as always already situated in our world.[25] Our world is structured in a meaningful way in which we act and live our lives.[26] We are always in a situation where things matter to us.

Where does mood come in? According to Heidegger, we're always disposed in some way toward the world.[27] This disposition or attitude toward things is our mood: the feeling of how we are in the world. He used the German word *Stimmung*, which refers both to mood and to the tuning of an instrument. As a result, the term *attunement* is often used to convey the way we are disposed toward things. According to Blattner, attunement is like a melody that sets the tone, and "we are tuned into the way things matter," and "our tuning, or our temper, is our mood."[28] We adopt this notion of mood as tuning in framing the central theme of the book.

Additionally, Heidegger views the world as arranged in particular ways, with attunements that our attunement can mesh with or not. In other words, not only are we tuned into the world; we are also tuned by the world.[29] This speaks to the way we are connected to the world—not as observers but as part of a whole. Furthermore, in Heidegger's view, moods are not private experiences. They are neither inside us nor outside us but rather act like an atmosphere in which we are immersed.[30] This speaks to the way moods may be public.

In a broader sense, mood can be akin to the sensibility of an age, the culture of a company, the temper of the times, and the mood of an individual at a particular time.[31] For example, cultures have long-standing sensibilities so that people

living within a particular society are conditioned to the moods of their culture. We also have social moods, and people of the same culture can adopt the moods of each other. No one is an island or lives in a vacuum.

Heidegger tried to capture what he meant by coining the word *Befindlichkeit*, meaning "how do you find yourself?" or "how is it going with you?"[32] The concept of *Befindlichkeit* is related to our "understanding" or how skillful we are in knowing how to act in a particular situation. We always possess some level of understanding, i.e., some ability or skill to deal with circumstance as we encounter them. We understand our world and ourselves through our practical engagements and the feeling-states that are fundamentally involved with these activities. As Heidegger puts it, every mood has its understanding and every understanding has its mood.[33] The concept of *Befindlichkeit* puts the person, body, and world together.[34] When we look at things this way, the significance of an event comes from the relation of the event to the person and his or her current concerns, and not from the intrinsic properties of the event. Certain feeling-states allow a person to view surrounding things as disclosing some, but not all, possibilities, putting the focus on the actions available to the person at any given time.[35]

From a developmental perspective, there is never a moment when a child is not involved in a situation—be it with family, or friends, or the classroom, or sports activities. At every step, the child possesses a degree of familiarity with, and a growing understanding of, his situations and tasks, as well as of his available options. Even a newborn infant is born into a situation and a world of possibilities. The newborn is born with her own attributes, her own tuning, her own unique degree of preparedness, into a particular family and culture with all the attendant worries, expectations, and hopes. The newborn also is faced with certain tasks, beginning with finding the nipple to nurse and advancing to ever more complex challenges that will be mastered to varying degrees, and at each level of mastery the baby will exhibit her mood.

One consequence of always being "tuned in" is that we experience the world in different ways at different times. What we find significant in a situation is a function of our mood, and our mood affects how we view the experience. For example, a sad or happy or anxious mood will lead us to experience a situation differently at any given time. *As you drive to work along the same streets, the sounds and sights you experience seem different depending on your mood. For a child on the way to school who usually seems carefree and bright, the same streets may appear dull and empty if her mood is sad instead of happy and cheerful.* Our

mood also gives life its sense of meaning, informing us about how things matter and how we're doing.[36]

Moods set up the world in which we experience feelings directed toward things or situations—in other words, emotions.[37] The following vignette captures what is intended, and illustrates a way of looking at the relation of mood and emotion. *John, a high school senior, has applied to college. The day for acceptance letters is approaching. He goes to the mailbox every day. He is not a disinterested objective observer of the contents of the mailbox. He is already in a situation. There have been years of preparation, hard work, and his and his family's expectations. He has been anxious for weeks; he approaches the mailbox with a feeling of anxiety and trepidation; he opens the box, and one letter seems to jump out at him. He recognizes the letterhead of his first-choice college. Everything else in the mailbox seems to recede—he does not notice anything about the other contents of the mailbox.*

John's mood has attuned him such that specific events or possible outcomes can and will affect him. Several possibilities are present in John's situation. The letter may say yes, it may say no, or it could say maybe. A "yes" answer would leave him joyous and contemplating a set of new and exciting possibilities, whereas a "no" would leave him disappointed and upset and with a diminished set of possibilities.

There are further implications of this approach to mood: We *feel* the significance of things and situations.[38] Mood provides a background sense of belonging to a world of meaning without which we cannot experience feelings about things, such as emotions.

Imagine a group of people who walk through a mountainous area during the early morning hours. Signs were posted one morning warning of mountain lion activity. One walker has heard of a confrontation between a hiker and a lion in the area. The behavior of the group begins to change: their hearts beat a little faster, their posture and pace change. One, who tended to be anxious and fearful, decides not to walk at that hour. Others carry sticks, and the group stays close together. The mood is fearful; everyone is watchful and alert to shadows and strange sounds. They are ready to respond with fear should anything even remotely resembling a lion appear.

We noted above that the significance of an event does not lie exclusively in its intrinsic properties but in the relation to the individual and the individual's current concern. An important implication of this notion suggests that mood is prior to cognition.[39] As events unfold, our mood (tuning) has already disclosed what is important to us and what possibilities are available before our cogni-

tive processes take over. The implications of this idea for cognitive theories of depression and cognitive behavioral therapy will be discussed in chapter 12.

MOOD, POSSIBILITIES, AND CHOICE

According to Heidegger, we are future oriented. We plan ahead, and in so doing we are moving into our possibilities. But our possibilities are always limited since we're not in full control of our situations. We must choose from the possibilities presented. A child may fail, may succeed, may plan activities with friends, or may make plans for high school or college—some of the many choices a child confronts all along the way to maturity.

Anthony, a high school basketball player, may dream of becoming the starting center of the Los Angeles Lakers. But if he does not grow to the requisite height then it's an unlikely possibility, and at some point he will need to select another career.

We have seen that our mood is intimately involved in determining what is significant versus our possibilities. Heidegger distinguishes between moods in which we are attuned to particular circumstances and fundamental moods in which we are attuned to the world as a meaningful whole.[40] Anxiety (angst) is Heidegger's primary example of a fundamental mood. As noted, we are future oriented (we plan ahead). We move into our possibilities, but our possibilities are limited just as our lives are finite, and we continue to move in the direction of death. How is this relevant to children and adolescents? Issues of mortality and the meaning of life often preoccupy adolescents. By nine years of age children express fears of death, and attempted and completed suicide remain serious problems in youth. Many acute and chronic illnesses of childhood carry the risk of death or shortened life span. Large numbers of children are raised in highly disruptive and broken homes, where they may have been abused and/or neglected. Other children are products of group homes or a succession of foster homes. These children are constantly faced with the questions *Who am I? Do I matter to anyone? Do I matter to myself? Do I have a future?* Some may even be unable to conceive of a future, let alone articulate one. The rates of disorders associated with mood remain very high in these populations.

Heidegger further states that the fundamental mood of anxiety can be awakened by the realization of our finitude, and he shows that mood clues us into our true possibilities. Most of us live in a world comprised by our social and cultural society, and within the confines of our culture we feel comfortable in

conforming to the expectations placed upon us. But when situations arise that awaken fundamental anxiety, our world and our very identity seem fragile and vulnerable.[41] We begin to recognize that the usual social structures, rules, and roles are no longer sufficient to guide how we live and that the significance of our world has disappeared or "withdrawn."

Heidegger implies that in these situations we no longer are faced with a set of possibilities and are free to determine our own decisions rather than do what is expected of us. In this form of anxiety the world of possibility is experienced as illusory, and we are free—or enabled—to make our own decisions (which comprise the concept of Heidegger's authenticity). To be authentic, we need to be ready and willing to grasp the fragility of our world and to do so with skill and focus.[42] In Guignon's words, we are "self constituting" and have responsibility for how we live our lives—"what we make of ourselves as we live our lives."[43] The authentic self becomes responsible for itself by how it engages with the world, its concern for others, and its responsibility for articulating its world.[44] This means we live inauthentic lives but need to "awaken" our attunements to attain authenticity.[45] The narrative we construct about ourselves may be right or wrong, and our mood (if we know how to pay attention to it) can and will reveal that something is wrong.[46]

The concept of becoming is borrowed from the writings of the German philosopher Friedrich Nietzsche, who advocated "Become who you are."[47] The process of becoming implies that the individual has characteristics and capacities, which in the interplay with life (making choices in situations) continually shape how a person is in the world. What does it mean for children who exist in the unsettled and unhappy world, as described above, to feel obligated to make choices and take responsibility for their lives? Most treatment interventions are directed toward helping children change behavior so they "fit in," as they are expected to behave in the society in which they live. While this may be essential for orderly function in society, interventions can go beyond this and help children from dysfunctional backgrounds to achieve a more self-constituting life. If the child's sense of what is possible can be changed, then mood can be changed, and if a new world of possibilities can be opened up then a more positive and peaceful mood can ensue.

To summarize, we have sketched how moods are equivalent to the feelings we have about the world around us and our sense of belonging to that world. Heidegger argued that, instead of being detached observers and acting on what we see, we find ourselves in situations that matter to us and where we can

interact with others. Mood is what makes things matter, and each of us remains tuned to the world in our own unique way. Our tuning is our mood, and our mood makes things matter by revealing and differentially disposing us to the possibilities presented. How things matter becomes the basis of our decisions, but mood is present before thinking and judging come into play. Conversely, emotions are feelings directed at something specific that go beyond mood in their cognitive and physiological components involving judgments and preparations to respond.

CHAPTER 3

MOOD AND DEVELOPMENT

This chapter highlights the development of moods and corresponding emotions that are relevant to the disorders addressed in later chapters. Particular attention is paid to interpersonal interactions, which are profoundly influential in the development of mood/tuning. By tracing the developmental connections between mood and relationships, especially with key caregivers, we lay the foundation for understanding how pathological moods may be related to the disruption or loss of personal relations. Chapters 4–6 will discuss the influence of relationships on the development neural circuits and the stress response. We also discuss unique and crucial developments in adolescence that are linked to increased rates of depression, especially in females.

INFANCY AND MOOD

We begin with infancy. A wealth of information exists to show that newborns and very young infants have sensory experiences. However, little empirical research has been conducted on infants' moods, since considerable ingenuity is required to determine what an infant is experiencing given their lack of language. It is far easier to study an infant's behavior toward specific objects than it is to study mood. Hence, almost all research on feelings in infancy focuses on emotion.

When newborns are given sweet-tasting substances they behave in ways that indicate acceptance.[1] For example, when a newborn is offered a sucrose solution he will suck in a burst-pause pattern. As sweetness is increased, he adjusts this pattern by sucking at a lower rate with longer bursts, more swallowing and higher heart rate. We can infer from this that the newborn can discriminate degrees of sweetness. But do newborns experience pleasure? Conversely, newborns given sour or bitter-tasting substances[2] or who are exposed to obnoxious odors grimace and attempt to reject them as evidenced by facial expression and

tongue and head movement.[3] Their actions suggest distaste and displeasure, but do they experience the corresponding feelings?

Moreover, neither sensory nor motor experiences begin at birth because the newborn already has experienced sensory and motor sensations as a fetus.[4] The fetus touches and grasps itself and sucks its thumb. It also swallows amniotic fluid and will continue to drink if the amniotic fluid is experimentally sweetened. Amniotic fluid also takes on the odor of food consumed by the mother. In addition, the fetus responds to sounds. This gives rise to evidence that fetal sensory experiences influence later behavior. Very young infants show a preference for tastes to which they were exposed during gestation or for a story read to them while still in the womb.[5] There is evidence that prenatal language exposure influences postnatal language preference and development.[6]

These studies suggest that fetal sensory experience registers, but does a fetus have feelings and experience moods that go along with sensory familiarity? We may not be able to answer that question, but are moods available at birth? Parents readily say their babies show typical moods from early on, whether peaceful or fussy, or irritable and cranky. If moods are present in the first few days of life, do they switch on at birth? What seems more likely is that the infant is indeed tuned to the world, and the substrate of tuning emerges in fetal life and continues to elaborate with development.

We can illuminate the issues involved by considering the role played by the sense of touch. Ratcliffe argues that touch is central to feelings about our belonging to the world or our relationship with the world. When we touch something, we not only feel *what* we touch but we also recognize the existence of something else. Perceptions of things that exist outside the body comprise a single experience. Ratcliffe makes the case that existential feelings (the term he uses to replace mood) have an analogous structure. They can be feelings of bodily states and/or ways of experiencing something outside the body.[7]

Similarly, Rochat describes how infants learn about their embodied self through playful self-exploration, which involves multimodal experience of bodily movements and actions they produce themselves. The manner in which infants actively touch themselves by clasping, waving their hands, and kicking and touching their legs and feet while vocalizing forms the basis for the infant's sense of its own body. These experiences also suggest there is an outside world, such as objects in the environment. In addition to what the infant gains from the experience of touch and other senses, it also feels its own changes in state—from calm to excitable, and the beginning of repetitive patterns. Rochat implies that the experience an infant gains about her own body during bodily movement and contact of self-exploration is inseparable from feelings about her own "vitality." Each forms a single experience. Such experience could be the basis for the infant feeling connected to the world and the beginning of feelings of how one is in the world.[8]

Stern also documents "vitality" affects. During the first two months of life, he theorizes that perceptions are "global" and are directly experienced as intensities, shapes, and temporal patterns. Distinctive subjective events accompany the variety of occurrences experienced by the infant. Such feelings arise when the infant moves, is touched, is picked up, is spoken to, or is dressed. Stern calls these associated feelings *vitality affects*, and adds that categorical affects such as joy, sadness, and anger contribute to the experience. The resulting nascent organization and global sense of the world is the basis for the emergence of the sense of self, forming the foundation for later development and awareness.[9]

Tronick is one of the few researchers to study mood in infants, and we note below his studies of the influence of depressed mothers' facial expressions on their infants. Some of his ideas are reminiscent of those derived from Heidegger. He suggests that moods can be organizing processes that structure behavior and experience over time, providing direction to the infant's behavior as he moves into his future. Infants are always cared for by others. They get picked up and held, and are cuddled, nursed, fed, and communicated with through voice and actions. During these connections babies are exposed to the emotions of those around them. Tronick suggests that moods are generated out of the infant's self-organized biorhythmic control processes, which interact with moods of the persons who share these situations with them. At another level, he suggests that moods are cocreated as part of a process of shared meaning with other people. Shared meaning lies in the interaction between the infant and its caregiver.[10] This is consistent with Heidegger's attunement as "the way of our being there with one another."[11]

INFANCY AND EMOTIONS

We saw in chapter 2 that emotions have cognitive and physiological components that prepare the individual to do something in relation to someone else or to a situation. Given a newborn's and infant's limited ability to judge and act, it is not surprising that different views are expressed on whether or not infants possess discrete emotions.

One view holds that distress and excitement can be identified at first, and

discrete emotions emerge later as the infant's motor, cognitive, and language capacities begin to develop. An alternate view is that basic, discrete emotions—each with its own profile—are identifiable in very young infants. According to Sroufe, emotions don't arise out of the blue but emerge from prototypic root forms present in pre-emotional reactions within the newborn, and anger, fear, and joy are not accessible to the infant until the end of its first year. Available emotions represent transformations of earlier "nonemotional reactions." The precursors are global reactions (excitement) to a wide range of stimulation that differentiate and become more specific over the first few months. The beginnings of a meaningful connection between stimuli and the infant's reaction result from its connections with the environment. At ten weeks, the relation of the infant to some event stretches beyond mere stimulation, and the infant seems aware of a meaningful relationship.[12] We could argue that the prototypes and precursors discussed by Sroufe represent the laying down of moods that enable the emergence of emotions. This also supports the idea that mood is prior to cognition, since they are present earlier in development.

Sroufe suggests the development of three basic systems: (1) the pleasure/joy system, (2) the fear system; and, (3) the anger system. During the newborn period, a wide range of internal or external events can lead to a physiologic state that is the prototype for each of the three systems.[13] These are the forerunners of later mature reactions. The behavior is reflexive, and one cannot readily distinguish reactions that would later be anger or fear. Sroufe does not consider them emotions proper because of the absence of meaning or subjectivity.

Pleasure, wariness, and frustration emerge after the newborn period. These are precursor emotions that have an element of meaning, and the content of the event plays a role. Diffuse reactions involving the entire body are based on general rather than specific meaning. The general meaning might be recognition or failure of recognition, or the disruption of an established motor sequence. These diffuse reactions can be difficult to distinguish except by intensity. Basic emotions such as joy, anger, or fear emerge during the second half of the first year. They involve an immediate, more precise reaction and have specific meaning. But precursor emotions are not extinguished, and pleasure, wariness, and diffuse frustration continue to occur. If we put this in terms of tuning, then what is happening is the emergence of moods that set the conditions for emotion to be possible as cognitive and motor abilities develop. Tuning becomes more precise and individualized as the infant gains experience, but broader more diffuse tuning is not lost.

In the next section we introduce the important construct of temperament that can also reflect how a child is tuned. Temperament is important for a number of reasons. Mood is a key component, it is the basis of later personality, and subtypes of temperament are predictive of later mood disturbance and disorders.

TEMPERAMENT AND MOOD

Even in early infancy, children can be seen to behave in characteristic ways as they interact with caregivers and their environment. This tendency to behave in typical ways while engaging with the world defines temperament. One early description of temperament refers to the "how" as opposed to the "what" of behavior.[14] For example, temperament encompasses how positive a child will be, how readily he becomes distressed, how fearful he is in the present, and how persistent he will be in pursuit of a goal. Temperament is relatively stable over time.[15] Children who tend to be negative in terms of mood and emotional reactions at age three are also inclined to be that way at age six. Conversely, children who tend to be positive follow a similar pattern and remain positive.

The relation of temperament to mood can also be seen in how temperament is measured. Three of six dimensions commonly used to classify temperament are indicative of mood: fearful distress/inhibition, irritable distress, and positive affect/approach.[16] Temperament is assessed by measures that tap into these tendencies as well as by measures of cognitive and behavioral characteristics. Moreover, these underlying indicators of mood have a relation to emotion, as research shows that there are stable individual differences in the tendency to express a corresponding emotion to a temperamental trait. Individuals who tend to be fearful are more predisposed to more intense episodes of fear.[17] The opposite is also true. Individuals who are low in fearfulness are less likely to show fear, or are likely to experience less intense fear. Similarly, individuals prone to irritability are more likely to experience frequent and more intense anger, whereas those low in the trait of irritability are less likely to experience anger and do so with less intensity.

Temperament is often conceptualized as having three components.[18] The first component, positive affectivity (PA), is characterized by positive moods (joy, happiness, enthusiasm, and pride), a high sensitivity to reward, and reflects a tendency to actively engage the world. The second component, negative affec-

tivity (NA), is characterized by negative moods (fear, anxiety, sadness), sensitivity to punishment, and avoidance and inhibition. The third component, constraint or effortful control, refers to the child's ability to suppress responses when there is conflict. This component reflects executive control of attention, the ability to delay gratification, and the capacity to control impulses and emotions.[19] Individual differences in temperament are thought to be present to some extent at birth, but effortful control only emerges at around age three.

Temperament and Personality

Personality speaks to individual differences in social and emotional functioning. Measures of these individual differences predict not only behavior; they also predict the quality of personal relationships and how individuals adapt to life circumstances, as well as happiness and health.[20] The three components of temperament are common to the main theories of personality. One suggestion is that personality is an amalgam of temperament and character, where temperament refers to individual differences in the tendencies underlying basic emotions, and character refers to individual differences in a person's unique goals and values.[21]

McAdams and Olson propose three developmental layers of psychological individuality. The layers are dispositional traits, characteristics adaptations, and integrative life narratives. They define dispositional traits as the broad, internal, comparative features of psychological individuality involved in consistencies in behavior, thought, and feeling across situations and over time. Traits are the fundamental dimensions of psychological functioning and are closely related to temperament. They write that we can look at the development of personality from three standpoints: the person as actor (behaving), as agent (striving toward goals), and as author (narrating). Beginning in infancy, temperament is the basis of later personality traits. In subsequent years, the child begins to develop goals and ambitions, laying the framework for the child as agent. The process continues in adolescence and early adulthood as the capacity emerges to create a narrative identity that helps create meaning in life.[22]

Two models are used to describe the range of identified traits. The Big 5 model has five factors: extroversion, neuroticism, agreeableness, conscientiousness, and openness to experience. Embedded in each factor are more specific traits. The Big 3 model has three factors: positive emotionality, negative emotionality, and constraint. Positive emotionality approximates extroversion, negative emotionality approximates neuroticism, and constraint overlaps with conscientiousness and control. Positive emotions are implicated in depression and manic states, and negative emotion in anxiety and depression, and they have their roots in infant temperament.

We can think of infant temperament as the substrate out of which personality traits emerge.[23] For example, the positive affectivity and approach evident in an early life may be precursors of the extroversion and positive emotionality factors of later personality. Similarly, neuroticism may be presaged by the anxious, fearful, or irritable distress that may emerge in infants. Similarly, the dimensions of early effortful control may presage conscientiousness and constraint.

Not only are individual differences in early temperament predictive of later personality, but they also predict the later emergence of disorders associated with mood disturbance. One particularly interesting group of infants and children is classified as behaviorally inhibited.[24] These infants and children demonstrate fearful distress and reticence when faced with novel or stressful situations. About 15 percent of infants and preschool children fit this category. Follow-up studies of behaviorally inhibited infants show that they are at later risk of developing anxiety disorders and depression. Infants can also be classified as having high-reactive or low-reactive temperament.[25] Highly reactive infants, who comprise about 20 percent of four-month-old infants, cry and arch their back or move vigorously when presented with unfamiliar stimuli in various modalities. About 40 percent of four-month-old infants demonstrate little motor activity or crying when exposed to the same stimuli. The two temperaments showed different patterns of moods and behavior and dissimilar physiological and brain activity. They also are differentially associated with the emergence of mood disorders over time. For example, the high reactive temperament is associated with the development of social anxiety.

In contrast to the behaviorally inhibited temperament, an exuberant temperament has also been identified.[26] The exuberant temperament is characterized by being sociable, a readiness to approach situations, and positive reactions to novelty. Exuberant infants show positive moods and social behavior, but in later childhood exuberance is associated with risk taking, impulsivity, fearlessness, and a tendency to be sensitive to reward. While exuberance is associated with better social skills, there is also a tendency to become frustrated when goals are blocked.

Irritability is another highly relevant element of temperament. Irritability has been measured in newborns[27] and may be prominent in some infants over the first two years. Although considered a principal mood,[28] irritability may be a hybrid of mood and emotion. It refers to being easily annoyed and touchy, but the behavioral manifestations are outbursts of anger and temper. This suggests that it may be possible to separate out a mood state (as defined in chapter 2), from feelings that are specifically directed at someone or some thing, i.e., an emotion. Irritable individuals tend to have a low threshold for frustration, especially when their efforts to reach a goal are interfered with.

Irritability may be a form of tuning that in the face of challenge manifests as anger, aggression, and temper outbursts. That alone will not make a disorder, but should the person also be tuned such that they are fearful, sad, or indifferent, then an anxiety disorder, depression, bipolar disorder, or antisocial behavior—or a combination of these—may emerge. In youth, irritability is included in the criteria for depression, bipolar disorder, anxiety disorders, and oppositional defiant disorder, but not conduct disorder. In adults, irritability is among the criteria for bipolar disorder, generalized anxiety disorder, as well as antisocial personality disorder.

ATTACHMENT AND MOOD

We saw in chapter 2 that we are always in situations that matter to us, and that mood reveals the available possibilities in these situations. Children are always in a situation, especially with others, and newborns enter a situation with total dependence on caregivers. One of the major social developments is the emergence of the infant's attachment to key caregivers. According to Bowlby, the infant has built-in biases to attach to a primary caregiver.[29] The caregiver provides a *felt* sense of security, a secure base, which the infant uses as a platform for exploration and learning. The resulting attachment increases the infant's chances of survival while promoting cognitive and emotional development. The degree to which the attachment is secure or insecure (reflected in the feelings of security) arises out of the interactions with the caregiver over the first few years of life. There is a normal sequence in the development of attachment. At around age four months, "wariness" of strangers emerges. Here the infant appears uneasy and unsettled when strangers appear. The onset of wariness marks a key step in attachment formation and is indicative of how the infant begins to discriminate

between caregivers and others. Wariness of strangers is followed at six to seven months by fear of strangers. Infants protest the approach of strangers and typically cling to their familiar caregiver. At around eight months, infants may cry or show signs of fear when separated from their primary caregiver. Here we see indications of the infant becoming aware of the possibility of separation or loss of her caregiver, and these possibilities can be unsettling and uncomfortable. For most infants, separation anxiety increases and then declines by around fifteen months.

Inherent in theories of attachment is the idea that the infant is forming a sense of the possibilities contained in relationships with primary caregivers. These possibilities include that caregivers are present in a regular predictable way; that they're always present when needed; or, conversely, that they are unreliable and may not return. Mood, as we learned earlier, reveals situational possibilities. Thus, the processes involved in attachment play a crucial role in the child's development of her sense of belonging to a meaningful world. There is experimental evidence that by the age of eighteen months infants can consider possibilities and that by three years of age can consider how things might have been different in the past.[30] But it is also possible that infants can consider possibilities at a much earlier age. Consider the following example.

A six-month-old infant meets her grandfather's brother for the first time. The grandfather and his brother are similar in appearance except that the brother has a beard. The infant, relaxed and comfortable in her grandfather's arms, stares at the brother. She then begins to look back and forth at the two faces, her lips tremble, and she looks uneasy and turns in to the grandfather when the brother approaches before tentatively looking back when he stops.

An infant's experience with caregivers has a major impact on the development and the quality of the attachment. Likewise, the degree to which a parent or caregiver is responsive, predictable, and reassuring plays a crucial role in how unsettled the child becomes. The quality of attachment has long-term implications for the development of anxiety and depression.[31] To understand how this is studied, it is helpful to review how attachment has been measured.[32] The classic procedure involves the observation of infants in controlled situations with their mothers and a few toys. First, the mother leaves, then a stranger enters, and then the mother returns. The child's behavior during each condition is recorded and scored. Infants typically fit in one of four categories: The first (and largest) group of infants comfortably explores and plays within their new setting and in the presence of their mother. They may become mildly distressed if she leaves and they are alone or if a stranger enters. Then

they resume their happy mood when she returns. These infants are scored as "securely attached." The second group of infants is clingy with their mother, explores less, and becomes distressed when left alone or with a stranger. These are rated as "insecurely attached." Some rebuff their mother when she returns, but others are ambivalent and may ignore her. A fourth group becomes very disturbed in the setting—angry, or aggressive, or they may freeze and not interact.

The degree to which an infant remains calm and is able to explores his environment or shows fearful or separation anxiety is dependent on a variety of factors such as temperament, prior experience, and parenting practices. For example, the behavior of category-four infants is linked to prior abuse.

Early attachment insecurity, as measured by behavior, modestly predicts increased risk for depression/anxiety, and the effects are stronger for preadolescent and adolescent youth.[33] The avoidant attachment subtype is related to later social withdrawal. Cognitive bias, difficulty with emotions, and self-concept may explain the links between attachment insecurity and depression/anxiety. Insecure attachment is also associated with coercive relationships with caregivers and later disruptive behavior.[34]

Irritability in infancy carries implications for the development of attachment. Irritable infants in the context of low social support available to their mother are likely to later be classified as insecurely attached, and they direct attachment behavior more often toward their caregiver.[35] Highly irritable and insecurely attached infants explore less, but interestingly, highly irritable toddlers were less sociable when insecurely attached, but more sociable when securely attached.[36]

Bowlby also identified loss of attachment figures as a potent risk factor for depression,[37] and this has been borne out in subsequent research in adults.[38] Bereaved youth also demonstrate an increased risk of depression,[39] whether or not the bereavement stems from natural causes or from an accident or suicide with the greatest risk occurring following the suicide of a parent.

DEVELOPMENT OF KEY MOODS AND ASSOCIATED EMOTIONS

In this section we sketch the development of some of the moods and their associated emotions that become the central features of the disorders to be examined later. We have seen from well-conducted sensory studies that

newborns may experience pleasure, and that smiles may indicate pleasure or happiness. Pleasure is more clearly evident at two months of age when an infant shows delight in response to her actions when pulled strings result in the sound of music.[40] A smile is the easiest and best indicator of pleasure and joy within the context of a positive mood. Smiling also illustrates the role that interactions with others play in shaping mood and emotional development. Smiles are more likely to be elicited by interactions with humans than by other interesting or novel things or activities. Social smiles, or smiles directed at people, are one of the first building blocks in the development of attachment between the infant and caregiver. Brief smiles can be seen during the first two to three weeks, but it is not until the third to the eighth week that discrete smiles in response to stimulation are observed. Social smiles directed at others are evident by the second to third month. This suggests that emotions, as defined earlier, are present around ten weeks. Expressions of joy are apparent by six months.[41] Over the course of the first year laughter emerges in response to a variety of situations, and we can infer that laughter marks an underlying positive feeling or mood.

By two months of age, observers can distinguish sad facial expressions from general distress, and by six months sad facial expressions occur in response to situations that elicit sadness.[42] Tronick showed the close relationship between parent appearance of depression and infant sadness by exploring how the infant's behavior changes when faced with a depressed mother.[43] Videotapes show that as the depressed mother fails to respond to the infant's efforts to engage, the infant begins to turn away, and his facial expression appears sad.

By two months, facial expressions of anger can also be identified and distinguished from sadness, and by four to eight months, anger can be identified as a distinct entity elicited by frustration.[44] Anger becomes increasingly common over the next two years as the infant learns to control her environment and encounters more opportunities to become frustrated. We noted above that infants show delight when their efforts at pulling a string produced music. But infants varied in their responses when their actions no longer produced music, sometimes showing anger and at other times exhibiting fear. One possible interpretation is that the tuning of the infant sets the conditions for her response to unexpected events—an irritable infant might experience anger, or a fearful avoidant infant might show fear. Cognitive development plays an increasing role in constraint.[45] Preschool-age children become angry if a peer harms them, whether or not the harm was intentional, whereas older children are less likely to become angry if the harm was unintentional.

Guilt is a complex emotion when it focuses on something done or on a behavior, involves feelings of remorse and regret, and there is a desire to make up for behavior.[46] Guilt can also be a mood or a feeling that is not explicitly linked to an event or person, and this is often the case in depression. Guilt arises when harm is done to another person; particularly if the harmed person is an attachment figure or someone closely associated.[47] As a result, guilt is frequently associated with estrangement from others or with the threat of loss and the anticipation of being punished or harmed. Studies reveal that guilt as inferred from behavior appears in the second and third year,[48] and children appear to understand the experience of guilt by age three.[49]

Worry and fear are related as both involve anxious thoughts, but they are distinguishable. Worry may be defined as repetitive, intrusive thinking about negative and aversive things that can but probably will not happen—it is concerned with future possibilities.[50] Worries in middle childhood are very common, tending to focus on school performance, dying, health, and social concerns. Fear is primarily concerned with anxiety that is elicited by the actual confrontation with some event or thing—it is concerned with real and present possibilities.[51]

Last has summarized the ages at which common fears become evident in childhood.[52] Before age two, separation anxiety and fear of strangers become prominent. But fear of high places and the fear of novel events (loud noises or looming objects) are also evident. Many of these fears emerge at seven months and decline around twelve months. Between ages two and three, fear of the dark and fear of small animals emerge. By age five, children begin to report fear of bodily harm and of "mean" or "bad" people. By age six, they express fear of supernatural beings, or of sleeping alone, or of events such as thunder and lightning. Between ages seven and eight, children express fears of events reported by the media. By age nine, fears related to school performance and physical appearance emerge. Interestingly, it is also the age when children report fears of death. The most common fears endorsed by nine- to thirteen-year-old children are of animals, particularly spiders, and of being kidnapped or injured.[53] These fears were related to specific incidents, and conditioning (associating the connection between an event and the fear) was the most common mechanism.

RECOGNITION OF MOODS AND EMOTIONS

The ability to recognize the moods and emotions of others is crucial to human behavior and is important to discussions of empathy and concern (see below). The capacity to recognize facial expressions is a key element in the development of this ability.[54] For example, salient expressions of emotion, particularly facial expressions of fear and anger, are rapidly detected and processed by the nervous system. These expressions are prioritized because they suggest the presence of threats to survival. Infants show a preference for faces during the first few months.[55] But infants don't discriminate facial expressions until they're five to seven months old because of functional limitations in the visual system. Interestingly, if both auditory and visual cues are used and not just visual cues, discrimination becomes evident earlier at three to four months.

Some expressions are more salient than others and appear to take precedence.[56] Five- to seven-month-old infants stare longer at facial expressions of fear, and they don't disengage from them even if distracting stimuli are revealed. These discriminatory abilities are shaped by not only the general experiences all infants possess (they see many faces and expressions) but also by specific experiences a particular infant may contain (exposure to abusive or hostile environments).

For example, the facial expression of a depressed mother shapes her infant's experience.[57] Researchers monitored infants interacting with their mothers who were asked to maintain a flat facial expression. Infants of depressed mothers tended to be less active and more withdrawn than infants of non-depressed mothers when they were face-to-face with their mother, and they protested less when their mother wore a flat expression. Experience coupled with genetic influences shape the underlying mechanisms. Individual differences in the degree of shaping may become predisposing or vulnerability factors for the emergence of anxiety and depression.

MOOD AND PRO-SOCIAL BEHAVIOR

The ability to identify and understand that another child or adult is experiencing a particular mood or emotion defines empathy. Empathy, sympathy, and concern are related topics that are basic to pro-social behavior, and are relevant to disruptive and antisocial behavior where mood may be indifferent or callous.

For example, empathy is said to be absent in a particular subset of youth with conduct disorder.[58]

Empathy can be defined by the capacity to experience the "emotional" state that is akin to or consistent with that experienced by another.[59] A child experiences empathy if she feels sad about encountering a sad child. Sympathy differs from empathy in that sympathy is a negative feeling a child feels when concerned about another. According to Prinz, sympathy is a feeling *for*, whereas empathy is a feeling *because*.[60] The experience of each child need not be the same. A child may feel sad because a friend is angry. Sympathy is focused on how the other is feeling. Moreover, he suggests sympathy and empathy are not emotions but rather are a process by which emotions come about and are directed toward something else. Concern is also a negative feeling that arises when another person is perceived to be in a bad situation or predicament. Concern differs from empathy and sympathy since it is directed at the predicament of another individual and not at the emotion or mood of the other person. As a result, Prinz suggests concern may be the more powerful and crucial motivator of helping behavior while empathy may not be a good motivator of pro-social behavior unless concern is also in the picture.

By the second and third years, children show interest when a peer is distressed.[61] But it is not until close to preschool age that clear evidence of helping behavior emerges. Pro-social behavior continues to increase throughout childhood and adolescence. There are strong family influences on the development of pro-social behavior. Modeling and teaching of behavior, providing opportunities to display pro-social behavior, and constructive and supportive parenting all promote sympathetic and empathic behavior. Genetic influences, perhaps mediated through temperament, are also likely to occur.

MOOD AND ADOLESCENCE

Cognitive and social development increases rapidly as the child continues to move into the world. Adolescence is a period of enormous development as adolescents begin to move away from their parents, spend increasing time with peers, and engage in community activities, volunteering, and service.[62] These social changes are linked to mood.

Negative feelings and emotions increase in early adolescence but decline toward late teenage years. Adolescents report they are happier when with their peers, and while early adolescence is marked by increased conflict between teenagers and parents, by late adolescence relationships with parents are less contentious. Why might this be so?

Moving toward peers brings adventure, uncertainty, danger, threat, and excitement, but it also means testing whatever felt security lay with parents and family as the adolescent experiments with new things that begin to matter to them.

Puberty brings about remarkable change. The influence of mood, which is particularly noticeable in early adolescence, may well be linked to pubertal influences. Nelson and colleagues suggest that the hormonal changes of puberty along with the maturation of neuronal processes and learning underlie the remarkable social changes that occur during adolescence.[63] Gonadal steroids influence responsiveness to social stimuli, particularly sexual responsiveness. New things begin to matter—relationships with others, especially romantic ones, but also relationships with peers, teachers, or coaches in which new ideas are tested and identities are forged. In a way, adolescence is a laboratory in which teen tuning (mood) reveals new possibilities, but the teenager's level of understanding and skill at negotiating the new challenges carries its own moods. While parents provide support and guidance, in many areas the adolescent is on his or her own and must decide among the possibilities that present themselves.

Casey and colleagues marshal data that suggests that younger adolescents, in particular, rely more heavily on feelings when determining critical personal decisions even though they may be capable of thinking rationally and logically.[64] Over the course of adolescence there's a gradual but marked improvement in reasoning and processing information that affords them new skills and expertise. The adolescent achieves a more fully conscious, self-directed, and self-regulating mind through the gradual establishment of executive functional capabilities.[65]

Further, a sense of self develops over the course of adolescence, transitioning from childhood and becoming more abstract, differentiated, and better organized over time. Research shows how an adolescent's self-view differs across contexts.[66] They view themselves differently with peers as compared to their view of themselves when in the company of parents or teachers. Interestingly, adolescents may project a false self, depending on the social context.[67] This false self is connected to mood, sometimes to please others, or to embellish their self-esteem, or to experiment with new situations, but if this self cannot be sustained or surmount challenges, then depression and hopelessness may emerge.

CHAPTER 4

MOOD AND NEURAL CIRCUITS

We suggested that mood is a phase of the activity of brain circuits and related bodily systems that are continually active as we go about our activities. The judgments made and resulting actions and accompanying bodily changes make up the emotions. This chapter discusses how information is transmitted in the nervous system, the brain regions and circuits relevant to mood and emotion, and the neurotransmitter systems that modulate the activity of the networks, and also sketches relevant findings on circuit development. In addition, the reader will see how these neural circuits are connected to key functions such as the stress response and the immune system.

We start from the concept that we perceive the world through our body.[1] Information is processed and stored, and action is initiated through the activity of the nervous system,[2] and these activities are performed by means of neural networks rather than through chemical formation and storage. We can think of mood as a functional state of neural networks: tuning/mood arises through the activity of neural networks and related body systems. Mood as a phase of their activity or tuning is always present as the circuits relay information.

While mood and emotion arise from coordinated activity in the circuits of the brain, it is premature to suggest how this happens. Can we separate out circuits for feeling, mood, or emotion as we have defined them? The answer is no. The difficulty partly stems from the fact that available neuroscience research typically focuses on emotion, and feelings and mood cannot be separated out. Can we separate out circuits for cognitive activities such as attention, memory, and problem solving from mood or emotion? Again, the answer is no.[3] Cognition and emotion are integrated in the brain and interact in complex ways. Brain regions viewed as related to mood and emotions are involved in cognition, and vice versa. Neural circuits may act as organized nested loops, and while each set of loops might underlie a particular function, the loops act as an integrated whole, while the individual responds to a situation.[4]

The brain is organized as a hierarchy.[5] More recently evolved cortical and subcortical areas participate in overall regulation and decision making. The lower and older parts of the brain regulate physiological and other functions that are necessary to maintain life. Historically, many of the areas thought to be involved in mood and emotion were referred to as the limbic system. This included the amygdala, hippocampus, the cingulate gyrus, and areas of the thalamus. However, the physical and functional boundaries of the limbic system are unclear, and today we know that many areas outside the limbic system are also involved.[6] For example, the prefrontal cortex (PFC) guides attention and cognition and inhibits inappropriate action, but it also regulates emotion. Regions such as the basal ganglia and nucleus accumbens are involved in motivational systems and motor activities.

NEURONS, SYNAPSE, AND CIRCUITS

The basic components of the nervous system are nerve cells or neurons, and nerve cells communicate and interact to form circuits that underlie all the activities of the nervous system.[7] There are a number of crucial ideas that permeate this and succeeding chapters, and they are the principles that guide how we can understand the ways we are connected to the world. Neurons connect at junctions called synapses; the synapse is the hub where change occurs. Vast numbers of interconnected neurons form circuits, and these are brain regions that perform particular functions. Activity in the circuits is regulated, and this regulation is the function of neurotransmitters. Crucially, environmental events not only influence activity in circuits; they also affect the development of circuits. The synapse allows these changes to occur. In other words, mind, body, and world are interconnected and inseparable. This chapter provides more detail on some relevant systems.

Neurons consist of three components: a cell body containing the nucleus; dendrites that carry information to the cell body; and the axon, which carries information away from the cell body. A fatty insulating layer, called myelin, allows an electrical impulse to travel along the axon and determine the speed of transmission. Neurons connect at the synapses, and groups of neurons form circuits. Information passes from neuron to neuron across the synapse and throughout the circuit. Electrical or chemical signals pass the information through specialized sites on the surface of the neuron at the synapse. These receptors recognize particular chemicals (neurotransmitters and hormones). Two neurotransmitters, one excitatory (glutamate) and one inhibitory (GABA, gamma-aminobutyric acid), are directly involved in the transfer of information from neuron to neuron. Transmission of signals—that is, how well a circuit functions—depends on the balance of activity between these two transmitters.

The synapse is central to the brain's functioning. Information is stored by a continual process of change in the relative strength of synapses. It is a hub where critical activities such as learning and memory take place. Mood disorders are treated by medication therapy that acts by changing the activity in the synapses. Plasticity, the capacity for change to occur in the nervous system, arises through activity in the synapses. For example, our ability to experience operates through its effects on plasticity.

OVERVIEW OF SELECTED BRAIN REGIONS

In the following sections, we sketch key features of regions involved in mood and emotion and in disorders that involve mood. Figures 4.1 and 4.2 show the location of these areas in the brain.

Prefrontal Cortex

The prefrontal cortex (PFC) (fig. 4.1) is central to executive functions, attention, coordinating responses to events (including the response to threat), and deciding a course of action.[8] Information about all aspects of the internal and external environment goes to the PFC. This makes the PFC central to intelligence and personality.

The PFC is located behind the forehead and contains specialized subregions that not only connect to each other but that also connect widely to other regions and systems. While medial and central areas may be involved in emotion, and dorsal and lateral areas in thought and action,[9] these functions are likely integrated.[10] PFC connections go to areas involved in autonomic, endocrine, and immune functions to provide bodily responses, and to motor areas to enable a person to act. For example, projections to the locus coeruleus (see below) and the ventral tegmental area (see below) connect the PFC to neurotransmitter systems. The connections are bidirectional, and neurotransmitter systems can influence the function of the PFC. As we will see in later chapters, the PFC is involved in regulating the stress response and is highly susceptible to damage caused by the stress response.[11] The PFC contains a number of regions that are

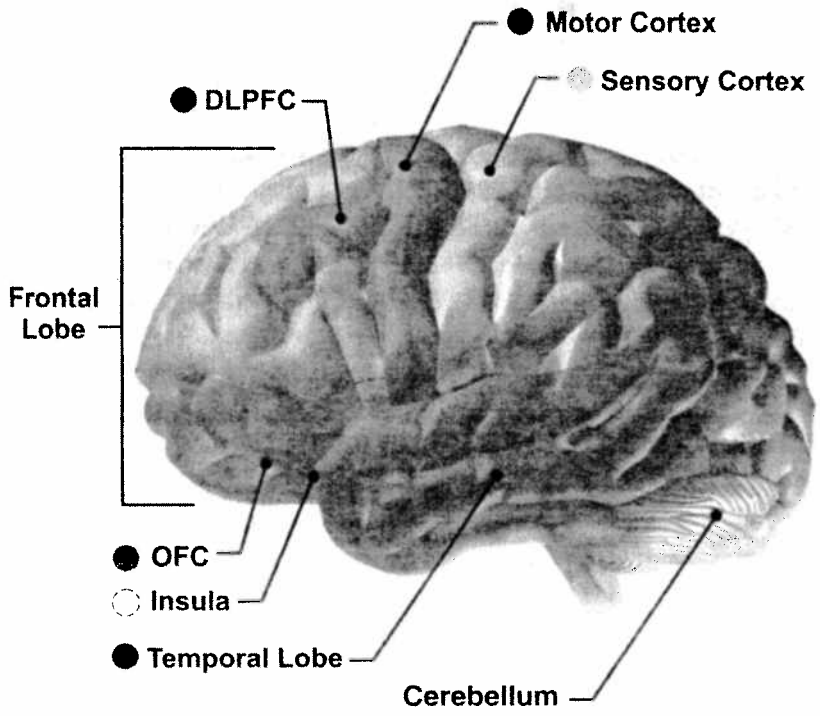

Figure 4.1. Lateral view of the brain showing key landmarks. Frontal area shows the dorsolateral prefrontal cortex (DLPFC) and orbitofrontal cortex (OFC). (Figure created by Dave Cantrell, Biomedical Communications, University of Arizona Health Sciences.)

involved in critical functions related to mood, emotion, cognition, and executive actions, and these are sketched in the next section.

The *orbitofrontal cortex* (OFC) (fig. 4.1) processes the affective quality and value of a stimulus, and influences and tunes perceptual processing in sensory systems.[12] This means the OFC is active when you're dealing with something you want to avoid, or dealing with something you work for or desire, and in learning to associate a stimulus and its reinforcers.[13] Thus, the OFC is involved in motivation (behavior involved in seeking rewards), and as we will see in later chapters this implicates the OFC in depression (decreased motivation) and mania (increased motivation). The OFC has direct connections to the amygdala (see below), is central to mood and motivation, and has reciprocal connections with lateral regions of the PFC, central to executive function.

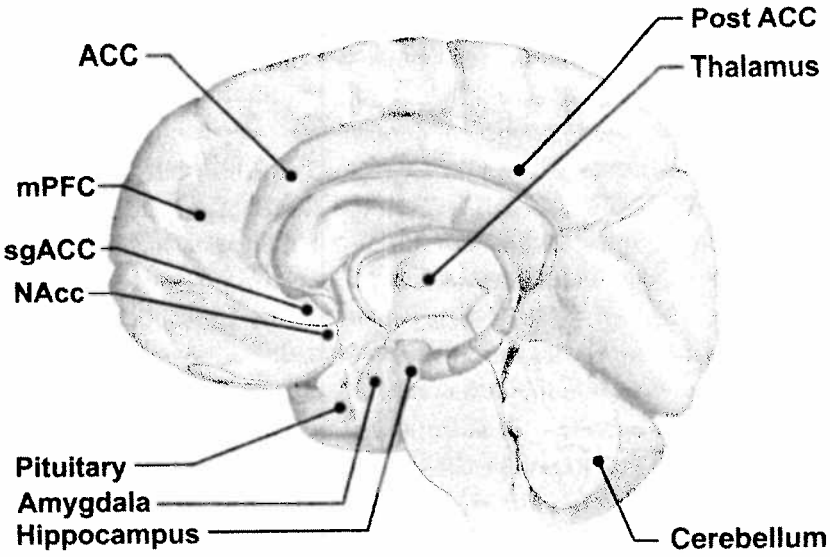

Figure 4.2. Medial surface of the brain showing the anterior cingulate cortex (ACC), posterior cingulate cortex (PCC), and subgenual ACC (sgACC). The medial prefrontal cortex (mPFC) is shown anterior to the ACC. Nucleus accumbens (NAcc) is shown in proximity to the sgACC. The hippocampus is shown in proximity to the amygdala. The thalamus is located centrally. The pituitary is close to amygdala and below the hypothalamus. (Figure created by Dave Cantrell, Biomedical Communications, University of Arizona Health Sciences.)

The *medial OFC* (mOFC) (fig. 4.2) may be involved in positive affective states, while the lateral OFC (lOFC) (fig. 4.1) may be similarly involved in negative affective states.[14] Furthermore, the mOFC may be involved in shutting down the response to fear and therefore implications for anxiety disorders. Not surprisingly, given these properties, the OFC is involved in recognizing emotions from facial expressions.[15]

But how is meaning processed? Roy and colleagues suggest that the *ventromedial* area of the PFC (vmPFC) functions as a hub that integrates information (mood- and emotion-related as well as cognitive and social) from other areas to provide meaning in situations for a person's physical and social well-being and future prospects. They base this notion on patterns of connectivity with other circuits and systems, such as those involved in memory, visceromotor functions, sensory information, and determining goals.[16]

Executive functions are processed in the *dorsolateral PFC* (DLPFC) (fig. 4.1), which is involved in setting goals and in working memory. Because of connections to the motor cortex and hippocampus, it plays a key role in coordinating behavior with circumstances in the environment.[17]

The *anterior cingulate cortex* (ACC) (fig. 4.2) further illustrates the complexity of the PFC. This is an area that can be thought of as a site where affect and cognition are integrated, and it further functions as a higher-level area where the physiological responses necessary to support cognitive and affective responses are generated.[18] The ACC in conjunction with the OFC and mPFC may be involved in processing the physical or physiological changes that accompany experiences with significant mood or emotional components. The ACC connects to the autonomic and endocrine systems involved in bodily symptoms that are associated with negative feelings and moods. Negative affect, pain, and cognitive control functions activate an area of the upper ACC, and information about reinforcers may be linked through this area to motor areas expressing affect and executing goal-directed behaviors.[19] The ACC may monitor the emotional salience of stimuli, influence the autonomic nervous system and cognitive activity, and as a result may influence responses when challenging events occur.[20] An area of the lower anterior portion of the ACC, the *subgenual* ACC, is implicated in depression and bipolar disorder (chapters 9 and 10). The involvement of the ACC in cognitive control or in constraining behavior implicates the ACC in temperament (see below).

Amygdala

The amygdala (fig. 4.2) lies in the medial temporal lobe close to the anterior tip of the hippocampus, and because of its many connections, the amygdala serves as a hub in mood, emotion, and social behavior.[21] The amygdala is a collection of nuclei with different connections.[22] The lateral nuclei are involved in processing input, learning connections, and associating events. The central nucleus connects the amygdala to areas in the cortex serving cognitive and executive functions, to systems regulating visceral or bodily functions, and to the motor systems serving action. Broadly speaking, novel and biological events are given affective significance in the amygdala, and although the amygdala preferentially participates in a range of negative experiences, it is also activated by positive experiences.

The amygdala gets information from the senses about the environment, as well as input about the internal state of the body. The input is multimodal, and

may include facial expressions, vocal sounds and intonation, posture, and movement.[23] The amygdala also connects back to sensory systems influencing sensory input and cortical processing of sensory input (e.g., the reading of facial expressions). The dopamine system (see below), the PFC gate sensory input to the amygdala,[24] and individual differences in these mechanisms may be related to mood.

The amygdala is primed to participate in tuning, to reveal situational possibilities and set the stage for how a person acts in situations. Consistent with this view, Cunningham and Brosch suggest that the amygdala is involved in determining the relevance of a stimulus and is activated depending on needs, goals, or values of the person.[25] Indeed, recent research suggests the amygdala is activated by the impact or subjective significance of events to the person. Moreover, it is closely associated with cortical regions thought to be involved in registering meaning in situations.[26] This finding is relevant to the idea (chapter 2) that mood makes things matter and reveals the significance of events.

Fear processing is one of the best-studied aspects of the amygdala's role in processing emotional expression.[27] This is an essential, rapidly processed component of the response to threat or danger. When a threat is perceived, the amygdala may inhibit the prefrontal cortex so that only essential responses occur. Cortical connections with the amygdala help take the context of the threat into consideration and may override any initial fear response. This ensures that the fear response is limited, and that the person does not live in a constant state of fear.

Not unexpectedly, the amygdala plays a key role in the processing of facial expression, especially expressions of fear, making the amygdala and its connections highly relevant to anxiety and antisocial behavior.[28] The subject need not be aware of the stimulus presented, and other indicators of fear, such as body posture or vocal expressions also activate the amygdala.

The amygdala, through its central nucleus, plays a crucial role in the response to stress and in regulating the neuroendocrine component of the stress response.[29] Circuits link the amygdala to visceral responses, the autonomic nervous system, and the stress response system (chapter 6). These connections may account for the physical or visceral sensations associated with anxiety, fear, and the response to stressful events.

Another way to look at the amygdala and tuning is through its connections to temperament.[30] There is strong evidence linking the amygdala with the tendency to avoid or to be inhibited and sensitive to negative aspects of situations. This suggests that individual differences in the excitability of the amygdala and its connections may underlie temperament. It also supports the idea that indi-

vidual differences in how the amygdala and related circuits function are key to the understanding of mood in the life of an individual.

Nucleus Accumbens

The nucleus accumbens (NAcc) (fig. 4.2) is a crucial component of the motivational reward system.[31] It serves as a crossroads between the limbic, cognitive, and motor systems through links to prefrontal cortex, amygdala, hippocampus, thalamus, and motor areas. Strong connections to the dopamine system (see below) give the NAcc a central role in positive states. The NAcc is activated by toned situations (humor, positive pictures, and verbal stimuli), and the anticipation of reward, which implicates circuits involving the NAcc in mood disorders.

Insula

The insula (fig. 4.1) may be involved in monitoring both the emotional and cognitive aspects of events. Craig has proposed that the insula in partnership with the ACC is responsible for our sense of awareness of others and of our environment and our sense of self.[32] Internal visceral sensations project to the insula and are then remapped as bodily feelings. This means the insula is involved in how aware we are or how sensitive we are to gut sensations, e.g., in anxiety or fear.

Hippocampus

The hippocampus (fig. 4.2) is a folded area at the base of the brain in the medial temporal lobes that controls short-term memory and conversion to long-term memory, and involves intellectual and emotional response.[33] The lower area of the hippocampus is primarily involved in behaviors related to anxiety, while the upper area is involved in the memory of facts and events. The amygdala connects to the hippocampus and may relay memories (especially emotionally charged ones) to the hippocampus for later retrieval. The hippocampus and amygdala play related, albeit different, roles in fear and anxiety as well as in negative affectivity associated with increased hippocampal activity.[34] It also plays an important role in the stress response (chapter 6).

Hypothalamus

The hypothalamus is a cluster of nerve cells that controls appetite and sexual and mood responses, located close to the pituitary gland (fig. 4.2).[35] It receives information from the amygdala, the cingulate cortex, the hippocampus, and also directly from the senses before transmitting signals to the endocrine and autonomic nervous systems. These connections allow the hypothalamus to integrate and coordinate essential life functions while offering explanations for body functions, which are altered in mood disorders.

Thalamus

The thalamus (fig. 4.2) is a paired structure close to the center of the brain.[36] Sensory information en route to the cortex passes through the thalamus where it is processed and organized into nuclei that process input from specific sensory or motor systems. The thalamus features in many key neural circuits because of the importance of its role in processing sensory information. Two circuits implicated in mood disorders link the thalamus, amygdala, cortex, and motor areas with other connections to the hypothalamus and autonomic nervous system.[37]

NEUROTRANSMITTER SYSTEMS

Neural circuits must respond and adjust rapidly when events occur. How is their activity adjusted? Neurotransmitter systems are mechanisms that have evolved to rapidly adjust the activity of neural circuits.[38] A neurotransmitter is a biochemical substance released by nerve endings that chemically transmit nerve impulses. Although these systems may originate in sites far from the brain, their transmitters are released in response to signals from the amygdala, OFC, ACC, and other areas. Widely distributed in the body, they work together by offering broad influence on the activity of neural circuits while ensuring that they play an important role in regulating body functions and response to stress. Psychotropic medications act through neurotransmitter systems (chapter 12).

Dopamine System

Dopamine is one of the most studied neurotransmitters in the brain. The dopamine system modulates the tendency to actively engage the world, affects sensitivity to rewards and the tendency to experience a wide range of positive moods.[39] As a result, dopamine is implicated in anhedonia (loss of interest and pleasure) and in motivation. The cell bodies begin in the ventral tegmentum, and overlapping dopamine pathways project too many key areas.[40] The mesolimbic (or reward) pathway projects to the nucleus accumbens, amygdala, anterior cingulate cortex, and prefrontal cortex. These areas are involved in monitoring the internal and external environment, generating moods, and corresponding emotional responses. As a further result, dopamine modulates the positive affectivity component of temperament.

Dopamine is released in the NAcc when significant events require engagement and adaptive responses.[41] The ACC receives more dopamine projections than any other area of the brain, while contributing to the ACC's role in approach behavior and the monitoring of rewards. Excess dopamine in the amygdala may heighten the response to threat while diminishing the influence of the PFC on the amygdala. This result could activate heightened fear responses. Individual differences in the capacity of the amygdala to store dopamine may also influence emotional processing in the amygdala and upper ACC.

Dopamine is also involved in the control of movement, and its depletion can lead to Parkinson's disease and motor function disorders. Its role in movement is important in producing side effects of psychotropic medications.

The dopamine transporter regulates the level of dopamine in the synapse. Certain enzymes, e.g., monoamine oxidase, metabolize dopamine, and genetic variations of these enzymes have important interactions with the environment that are linked to mood and other disorders.

Serotonergic System

The serotonergic system is involved in mood, learning, memory, and regulating vigilance.[42] This system begins in the midbrain and sends projections upward to a variety of structures that include the cerebral cortex, PFC, limbic areas, hippocampus, and thalamic nuclei, where the transmitter serotonin is released by nerve endings. The serotonin transporter is under genetic control[43] (chapter 5) and results in a short and long form of the serotonin transporter. Significant

interest has been focused on the short or "s" allele. Those with the "s" allele show reduced volumes of the ACC and amygdala. Having the "s" allele increases vulnerability to stress (chapters 5 and 6) and makes the amygdala more responsive to input through its effects on the circuit-linking PFC and the amygdala. A more responsive amygdala is receptive to environmental input that can lead to increased anxiety or sadness. The "s" allele is associated with depression in the context of early abuse, neglect, and traumatic events.

Noradrenergic System

The noradrenergic system (NA) helps maintain vigilance, facilitates shifts in attention and memory, is active when an individual is adapting to a changing environment, and helps regulate the fear response.[44] The noradrenergic system originates in the midbrain as a group of neurons called the locus coeruleus (LC). The LC connects to the spinal cord and brain stem, as well as to the thalamus, hypothalamus, hippocampus, and cortex. Norepinephrine is increased during stress (chapter 6), and chronic stress sensitizes the response with the result that subsequent acute stress produces a more intense response. The LC has significant influence on the amygdala, where it can lower the threshold for future activation.

CIRCUITS RELEVANT TO TUNING

There is a voluminous and ever-expanding literature on the relevance of brain areas and systems to mood, emotion, and behavior. One prominent approach is that of Price and Drevets.[45] They describe two basic systems, which serve essentially as an input and an output system. The input system (or orbital network) is comprised of areas in the orbital PFC, receives sensory input, assesses objects, and is also critical in anticipating reward. The output system (medial prefrontal network) includes areas in the medial prefrontal cortex as well as some areas in the OFC, ACC, and the vmPFC. As an output system it connects to neuroendocrine and autonomic systems and to motor systems. The amygdala and other limbic structures have critical bidirectional connections with the medial network. This framework provides a structure illustrating how these areas collaborate to maintain normal function, and it provides a basis for understanding how the various clinical symptoms and behaviors of the disorders involving mood emerge.

We can also think in terms of interconnected systems that generate mood and emotion, regulate the processes that underlie them, and underlie reward-seeking behavior.[46] The medial prefrontal cortex, anterior cingulate, and OFC are involved in processing emotion and in the automatic regulation of emotion. Cognitive control and effortful regulation of emotion involve the lateral PFC, including the ventrolateral and dorsolateral areas. The amygdala and ventral striatum are involved in reward processing as well as emotion. The connections among these areas result in a medial prefrontal-limbic network that includes the amygdala, anterior cingulate, and medial prefrontal cortex. This system is modulated by serotonin. A second system can be conceptualized as a reward network system and includes the ventral striatum, orbitofrontal cortex, and medial prefrontal cortex. The reward system is modulated by dopamine.

Fear Circuit

Circuits underlying fear are among the most researched and important circuits in the nervous system. They underlie the systems involved in processing threat and are involved in anxiety disorders.[47] Key components include the amygdala, an area called the bed nucleus of the stria terminalis (BNST), and areas of the prefrontal cortex. The amygdala appears to be critical for the production of fear as part of its overall role in processing mood and emotion. The amygdala in this context seems to be necessary for learning the associations between stimuli and reinforcement. The BNST appears to be involved when fear is sustained over time and is also involved when threats are less specific and less predictable. The PFC participates in both automatic regulation and when effort is required to regulate responses. With regard to fear, the vmPFC is involved in inhibiting conditioned fear and in the extinction of conditioned fear. Lateral areas of the PFC (e.g., DLPFC) participate in regulating fear responses through their role in attention.

The circuits involved in fear arise through connections between these areas, as it is thought that the PFC modulates the amygdala. Anxiety disorders are hypothesized to result from an imbalance between production of fear through the amygdala and inadequate regulation through the PFC (chapter 8).

Reward Circuit

The reward system underlies motivation, goal seeking, novelty seeking, and reinforcement of behavior and is centered on dopamine, the nucleus accumbens, and their connections.[48] Dopaminergic projections originate in an area known as the ventral tegmentum (VTA) and go to the nucleus accumbens, prefrontal cortex, amygdala, and hippocampus. The VTA is modulated by input it receives from the nucleus accumbens, prefrontal cortex, and amygdala. The serotonin system also modulates the dopaminergic projections through projections to the nucleus accumbens and the VTA. The nucleus accumbens in turn projects to the globus pallidus in the basal ganglia, and projections then go to the thalamus and back to the prefrontal cortex. These circuits underlie positive emotions and have become a critical focus in understanding the emergence of mood disorders and anxiety in adolescents.[49]

Decision Making and Executive Action Circuits

In making decisions we not only draw on our past experience and our current goals but we also anticipate future outcomes. Decision making is a complex process and is influenced by emotional tone and cultural context. A number of models of decision making have been proposed. For example, Rosenbloom and colleagues suggest decision making involves circuits in the cortex and their connections to the amygdala, hypothalamus, striatum, thalamus, and other areas.[50] Within the cortex, the key areas are the OFC, the ACC, and the DLPFC. The OFC monitors rewards and punishment, and different subareas are specialized for different levels of reward, and it is involved in networks responsible for emotional processing. The DLPFC participates because it is involved in planning and other executive functions. The ACC is involved when situations are conflicting and choices are ambiguous. The OFC has outgoing connections to different areas of the amygdala that lead in one case to autonomic arousal by disinhibiting the hypothalamus and a second output leads to inhibition of the hypothalamus. Further connections go to the striatum, which connects to the thalamus and back to the cortex. Lesions in this circuit may lead to disinhibition, lability of behavior, alterations in reward-seeking behavior, and apathy.

TEMPERAMENT AND NEURAL CIRCUITS

Temperament (chapter 3), or the tendency to behave in typical ways while engaging with the world, is an important construct. From early infancy, children can be seen to behave in characteristic ways as they interact with caregivers and their environment. Temperament becomes a significant component of later personality. As we have seen, temperament is related to mood. Temperament is also a model situation illustrating how neural networks might combine to produce the mood and behavioral tendencies that make up temperament types. To recap, temperament is often thought of as consisting of negative affectivity, positive affectivity, and constraint or control. Whittle and colleagues propose that specific neural circuits underlie temperament, and individual differences in the dimensions of temperament may depend on how the connections function.[51] Negative affectivity, or expressed or felt frustration/anger when limits are set, is associated with a circuit linking the amygdala and lower ACC with structures in the right hemisphere. These include the hippocampus, the upper ACC, and dorsolateral PFC. The amygdala and lower ACC are involved in the production of affective states, as well as the appraisal and regulation of autonomic responses to affective experiences. The right hemisphere structures are more involved with executive functions, integrating cognitive processes, affective input, and the effortful regulation of affective states. Whittle and colleagues established that smaller volumes of regions in the ACC were linked to negative affectivity in adolescents.[52]

Positive affectivity is associated with a left-sided circuit based on the NAcc getting input from the amygdala, and with the hippocampus and lower ACC being less involved. Projections from the NAcc to left PFC (including upper ACC and dorsolateral PFC) promote conscious feelings of pleasure, and they influence the drive to engage in pleasurable activity. The prefrontal regions in return regulate affective processing in the NAcc and amygdala. In adolescents, the volume of ACC subregions was linked to seeking out and enjoying intense experiences and affiliative tendencies.

The circuit underlying constraint or effortful control is hypothesized to involve some or all of the above structures. They suggest that constraint is positively related to how much inhibitory control is exerted on the amygdala and NAcc by the dorsal ACC, DLPFC, and lateral OFC.

CHAPTER 5

GENES, ENVIRONMENTS, AND NEURAL CIRCUITS

In this chapter we consider the role played by genes in forming the circuits underlying tuning and then examine how genes and environments interact in shaping circuits and the way they function. First, we sketch the basic principles of how genes operate, and then we discuss current thinking about how environments and genes interact, especially in development. This will give insight into processes underlying individual differences in tuning that are important to the development of resilience, vulnerability, and mood disorders. We will see the important role relationships play in these interactions.

GENES AND WHAT THEY DO

Genes encode for proteins (strings of amino acids) that form the building blocks of the body, regulate the function of neurons, and make peptides that are the means of communication within and between cells.[1] Variations in these genes have a profound influence on development and function. Current evidence suggests that the environment regulates the cellular signals controlling the genome such that the way cells function is the result of a constant dialogue between the genome and its environment.

How does this work? The basic genetic information is carried in the DNA. The DNA is contained in the cell nucleus in forty-six pairs of chromosomes, each pair made up of a chromosome from the mother and one from the father. The information is contained in long strings of chemical bases arranged in a double helix. There are only four bases (adenine, thymine, cytosine, guanine) arranged in sets of three. The three base sequences make up the code (the instructions) to make proteins or peptides. A gene refers to a section of the string of bases that contains particular information.

Protein manufacture begins with DNA directing the synthesis of messenger RNA. An exact copy of DNA nucleotide sequence information is read. This process is called transcription. The messenger RNA then directs the synthesis of amino acids leading to the formation of proteins. This process is called translation. Both transcription and translation are key to our understanding of how change can occur in neurobiological function.

Gene expression refers to the selective activation of genes and involves both transcription and translation. Genetic and environmental factors influence the processes involved in transcription. Genetic influences that affect transcription are referred to as the "promoter." These are sequences of bases that can regulate a gene. Changes in gene expression can result from mutations where bases are deleted or otherwise modified. While only one gene codes for a particular protein, there are multiple genetic influences on its transcription and expression. The same gene can also produce a number of different proteins via a process known as splicing. Genetic polymorphism refers to changes in the bases coding for a particular protein.[2] These genetic polymorphisms may give rise to different amino acids and can change the way the protein functions. Because of this, polymorphisms play very important roles. For example, the effects of polymorphisms on brain circuits and synaptic activity are the basis of genetic influences on the stress response and gene-environment interactions (see below).

But changes in gene expression can also be brought about without changing the underlying DNA sequence. Environmental (nongenetic) influences can change gene expression. Epigenesis refers to modifications made to the DNA or to regions surrounding the DNA by chemical means. For example, adding methyl groups to a base affects the transcription of a gene. Epigenetic processes are important because they are the means whereby environmental influences work. Early life events can influence the epigenetic state of parts of the genome, modifying the way genes build proteins.[3] For example, animal studies suggest that a mother's behavior toward her offspring can bring about stable changes in gene expression. Such epigenetic influences may become the basis for individual differences in behavioral and neuroendocrine response to stress in adulthood,[4] and subsequently may result in individual differences in the risk for psychopathology. This important work shows that relationships play vital roles at the very basic level of gene expression, and that they thereby influence neural circuitry that underlies mood.

Of further importance, gene expression is specific to periods of development as well as to specific issues.[5] Certain genes are activated during fetal life,

leading to the formation of new nerve cells. Genes regulating the development of connections between cells are active during early infancy. Other genes are activated during adolescence when further brain growth occurs. The early construction processes seem to be primarily genetically controlled, while the later processes of connecting and expanding are more influenced by the environment. The next section explores key issues in how genes and environments interact and the differential effects of environmental influences in infancy and early childhood and adolescence.

GENES AND ENVIRONMENT

Genes and environmental factors play a role in producing individual differences in behavior.[6] All children in a family share certain things, but each child will also share unique environmental influences. It appears that it is these non-shared environmental influences that are important in making children different. Environmental influences (e.g., parenting or social support) also have strong genetic influences because we select, modify, and construct our own world experience. Genes and environments also interact where there is differential exposure to experiences, and this type of interaction is the basis of diathesis-stress models (see below). Genetic factors that affect one trait may also affect other traits, and recent studies of the strength of this correlation have led to the idea that there are generalist and specialist genes.[7] The basic idea is that certain genes have broad effects, and the unique environments individuals experience determine final functioning. For example, in relation to the focus of this book, studies show that psychopathology can be divided into two broad domains of internalizing disorders (anxiety, depression) and externalizing disorders (disruptive behavior), and these broad domains share common genetic factors. The notion is that generalist genetic factors lead to the broad dimensions, and then other genes provide the specialist environments that shape the final form of the disorders that present in a particular individual. The overlap of anxiety and depression, the overlap of irritability and disruptive behavior and depression, and the overlap with disruptive and antisocial disorders are three areas relevant to mood where such ideas may apply. These ideas can be construed as consistent with tuning, with generalist genes setting the basic templates of the range of moods we experience, and specialist genes influencing the particular mix of moods that are characteristic of a given individual.

GENES, ENVIRONMENT, AND NEURAL CIRCUITS

With this background on genes and environments, we can now consider the development of neural circuits that are the basis of tuning. The growth of circuits depends on genes and environmental input working together, and neuroplasticity allows the connections (and communication) between neurons to respond to experience.[8] The next chapter considers how stress affects circuits and development.

Two great developmental events occur during the growth of neurons and their connections.[9] Massive growth occurs before birth and continues into maturity, but more connections than necessary are established during this time frame. Two waves of pruning occur. About 40 percent of synapses are pruned back in the early wave in infancy, and a second wave of pruning occurs during adolescence. The process of pruning has significant implications for our understanding of the effects of experience. While genes control brain growth, pruning is influenced by experience. The effects of experience on brain development can be classified as experience-expectant plasticity and experience-dependent plasticity.[10]

In experience-expectant plasticity, the brain "expects" certain experiences to occur. Every infant and child are exposed to a myriad of experiences that shape the structure of the brain. For example, infants are picked up, they hear, see, smell, and touch things, all of which affects brain growth. Connections between neurons that are most used survive, and those that are less active are pruned. Experience-expectant plasticity offers both a positive and a negative side. While the brain can recover from damage by having other areas take over functions, the absence of expected experiences leaves the developing brain vulnerable to damage. For example, there are sensitive periods during which exposure to certain experiences need to occur. Otherwise, the circuits do not develop normally and the relevant functions do not emerge. The classic example is the effect of experience on the developing visual system, where, for example, exposure to horizontal lines during a certain period is critical, otherwise the animal loses the ability to see horizontal lines later.[11]

In experience-dependent plasticity, the unique experiences of each infant or child affect brain growth. Here, the neural connections are made and reorganized based on the individual's unique experience. For example, being raised in complex environments leads to greater and stronger connections and improved performance. But if a child is exposed to an impoverished environment, deleterious effects are likely.

With this background understanding of genes and gene-environment interactions, we can consider the development of key regions and circuits that are involved in mood and emotion.

DEVELOPMENT OF CIRCUITS INVOLVED IN MOOD

The amygdala steadily develops throughout gestation, and there is evidence that it is well formed and functional at birth.[12] By ten months of age, connections between the amygdala and the cortex are myelinated. This early myelination of the connections between the amygdala and the cortex coincides with the emergence of stranger fear and separation anxiety in infants. Moreover, the development of connections between the amygdala and orbitofrontal cortex (OFC) is related to infants' capacity to recognize facial expressions as they are exposed to social signals.[13] The neural circuitry enabling a child to recognize facial expressions appears to be active early in infancy.[14] Over the course of childhood, the developing amygdala is involved in learning the meaning of facial expressions. This is especially relevant for expressions of fear, anger, and threat. The volume of the amygdala continues to increase during adolescence and into the twenties. Between four and eighteen years of age there is a significant increase in the volume of the right amygdala in boys, but not in girls.[15]

Growth of the prefrontal cortex (PFC) follows a protracted course, and reward-related circuits involving the PFC show marked changes during adolescence.[16] The frontal cortex grows rapidly from mid-childhood until adolescence, mirroring cognitive development and emerging executive functions. Synapses in the PFC proliferate during childhood and on into puberty, and the second wave of reorganization and pruning occurs in adolescence. Myelination also increases into adolescence, and the combined processes lead to improved prefrontal connectivity.[17] Larger volumes of left OFC and hippocampus are associated with higher effortful control or the capacity to constrain behavior in adolescents.[18] We saw in chapter 4 that the anterior cingulate cortex (ACC) is an important region of the PFC, but although it is identifiable at eighteen weeks gestation, little is known about the development of the ACC in humans, except it appears that myelination in the ACC continues throughout life.[19]

The relative rates of development of different regions have interesting implications, as presented by Casey and colleagues.[20] For example, ventromedial areas of the PFC develop earlier than lateral prefrontal areas, suggesting that areas

processing meaning, significance, or the impact of events develop before executive control. Furthermore, although connections between the amygdala and the PFC develop rapidly during adolescence, development of the frontal cortex lags behind the amygdala. The protracted development of the PFC is associated with the decrease in impulsivity that occurs with increasing age, spanning across childhood and adolescence, leading to the interesting proposal that greater risk taking in young adolescents relative to children or adults is related to the relatively greater development of the amygdala and associated circuits in early adolescence. A further suggestion is that the nucleus accumbens, involved in reward circuitry, is activated along with the amygdala when adolescents make risky choices and may play a role in risk-taking behavior that is especially high in the presence of peers.[21] Supporting this notion is the observation that when adolescents are engaged in a task where reward is anticipated, relatively greater activation occurs in the nucleus accumbens relative to the prefrontal cortex.

Pubertal influences also come into play. Gonadal steroids regulate neurotransmitters, thereby affecting circuits involving the amygdala and social behavior.[22] The earlier development of the ventromedial PFC relative to lateral PFC areas is dependent on experience and is less influenced by gonadal steroids.[23] The late maturing of prefrontal regions in adolescents (and, therefore, lessened capacity to self-regulate or exercise control) may leave adolescents vulnerable, particularly to the emergence of anxiety.[24]

Neurotransmitter systems regulate circuits and also show developmental patterns. For example, the dopaminergic system develops substantially in adolescence.[25] The developments mirror the pattern of growth and pruning as projections to PFC increase and are pruned. But pruning is less pronounced in the PFC, and this results in a relative dominance of the mesocortical connections, involved in motivation. One result is that the adolescent can now become motivated by more abstract and complex goals and rewards.[26]

The relation of infant characteristics to adult brain function can also be seen in studies of infant temperament. Infant temperament measured as early as four months of age is related to structural differences in the orbital and ventromedial PFC of adults.[27] Infants with low-reactive temperament compared to infants with a highly reactive temperament showed greater thickness of the left OFC, whereas highly reactive infants showed greater thickness in the right ventromedial PFC. Moreover, a highly reactive infant temperament predicts greater amygdala reactivity to novel faces in adults.

GENES AND SUSCEPTIBILITY TO PSYCHOPATHOLOGY

The genes that bring about susceptibility to psychopathology are very common.[28] They are normal alternate gene variations or alleles. The risk associated with these allelic variations is low and is on a continuum rather than acting in an all-or-none fashion. Linking genes to discrete psychiatric disorders, however, is extremely difficult. We have seen how complex mood and emotion are. Behavior also is complex, and psychiatric disorders are heterogeneous, making measurement extremely difficult. Moreover, genes act on molecular and cellular mechanisms of information processing in circuits,[29] and as a result, the effects of genes on behavior are indirect. The next section examines the role of genetic polymorphisms.

Polymorphisms and Neural Circuits

Studies linking common polymorphisms to neurotransmitter function are one widely used pathway relevant to understanding how tuning comes about. The neurotransmitters serotonin and dopamine have been the subject of many studies.[30] For example, a common polymorphism resulting in short and long alleles occurs in the promoter region of the serotonin transporter protein 5-HTT. These alleles, short and long 5-HTT, produce their effects by regulating the amount of serotonin in the synapse, where the efficiency of serotonin regulation is affected by the short allele. Serotonin neurotransmission is also dependent on a monoamine oxidase A (MAOA) enzyme for which polymorphisms exist, one of which produces a low-activity enzyme. Dopamine neurotransmission in the prefrontal cortex is affected by a polymorphism in the gene for an enzyme, catechol-O-methyltransferase (COMT), which inactivates dopamine, potentially affecting cognitive function and decision making. One allele produces a low-activity enzyme. A second key polymorphism occurs in the dopamine D4 receptor and may affect behavior related to reward seeking.

Another way polymorphisms can act is through effects on the amygdala and other brain areas involved in mood and emotion. The short allele of the serotonin transporter protein has been linked to reduced volume of gray matter in the amygdala and cingulate cortex, and it has also been linked to the degree to which the amygdala is activated by negative stimuli and to the degree to which the amygdala is coupled to PFC activation.[31] The low-expression MAOA polymorphism is also associated increased responsivity of the amygdala but reduced

reactivity of prefrontal regions.[32] Of further relevance to the idea that our tuning reveals what matters to us and the possibilities in situations, polymorphisms affect the circuitry that underlies responses to fearful and angry facial expressions. For example, those with one or two copies of the short allele of the 5-HTT polymorphism showed greater amygdala activation to threatening facial expressions than did those homozygous for the 5-HTT long allele.[33]

Polymorphisms and Temperament

The complexity of gene-environment interactions can also be seen in the development of temperament and in the role temperament may play in the emergence of disorders. While individual differences in temperament are partly due to genetic influences, the environment plays a large part in determining whether children with a particular temperament get into difficulty or develop a disorder. Moreover, personality development appears to be a lifelong process that is subject to genetic and environmental influences.[34] The environmental influences on personality vary by age and include changing social roles (e.g., entering the workforce, marriage) and individual life experiences. Genetic influences may be more important in the early decades, and environmental factors play a role throughout.

Polymorphisms are relevant to temperament. Individual differences in aspects of temperament have been linked to two important receptors in the brain.[35] Infants who have the short rather than the long allele of the dopamine DRD4 gene are rated by their mothers as higher in negative emotionality at two and twelve months of age, and infants who have the short 5-HTT allele tend to be more behaviorally inhibited and show heightened fear. Infants with the short form of both alleles show more negative emotionality than infants who carry only one risk allele. The principle that genes appear to have indirect effects and that they produce their full effects only in the presence of particular environments is relevant here, and we again see the influence of relationships. The child's relationship with her parents and the parents' socialization practices play an important role in shaping a child's temperament.[36] For example, children who tend to be in negative moods and who are also avoidant and sensitive to punishment do less well if their parents are punitive and rejecting.

CHAPTER 6

WHEN EVENTS THREATEN STABILITY—THE STRESS RESPONSE

In this book we suggest that moods emerge out of coordinated activity of neural networks that are constantly working as we interact with the world. We examined aspects of the development of circuits and the ways genes and environments function and influence circuits. We now consider what happens when events threaten stability, and how such stressful events shape neural circuits. First, we outline the stress response and key factors that influence the development of the response. We examine the effect the stress response has on neural networks, vulnerability, and resilience. Here we see that relationships with others are among the more profound influences shaping the stress response and, therefore, on the neural circuits and the moods they support. Moreover, we will see how the stress response plays crucial roles in the emergence of individual differences in key systems.

WHAT IS STRESS?

Stress is a subjective sense we have that something adverse is likely to happen and that our well-being is threatened.[1] It is important to note that any event, positive or negative, is potentially a stressor if the event is likely to disrupt a person's overall balance or homeostasis. A change of job or school might be a stress for one person, but not for another. The loss of a loved one or even the possibility of the loss of a relationship that matters to us, or changes in health or status, or expectations placed on us are stresses just as much as are physical threats to safety. Threats may be imminent (the sudden appearance of a snarling dog), requiring immediate action, or they may be in the future (consequences