second edition

Handbook of PRESCHOOL MENTAL HEALTH

Development, Disorders, and Treatment

edited by Joan L. Luby

ebook

THE GUILFORD PRESS

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To my father, Elliot D. Luby, MD,
the first and wisest psychiatrist I have known
and my mentor in this field and in all matters of the soul

About the Editor

Joan L. Luby, MD, is the Samuel and Mae S. Ludwig Professor of Psychiatry (Child) at Washington University School of Medicine in St. Louis, where she is also founder and director of the Early Emotional Development Program. Dr. Luby's research focuses on preschool mood disorders, particularly depression—its clinical characteristics, biological markers, and associated alterations in brain and emotional development in young children with depressive syndromes. Another key area of interest is treatment development that focuses on early psychotherapeutic intervention, sensitive periods, and neural markers of change. Dr. Luby's contributions include establishing the criteria for identification, validation, and early intervention in depressive syndromes in the preschool age group, as well as studies showing the effect of parental nurturance and early experiences of poverty on brain development. She is a recipient of honors including the Gerald Klerman Prize for Clinical Research from NARSAD (now the Brain and Behavior Research Foundation) and the Irving Philips Award for Prevention from the American Academy of Child and Adolescent Psychiatry. Dr. Luby has published extensively in general and child psychiatry journals and serves on a number of editorial boards.

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Preface

Since the first edition of this handbook was published in 2006, there have been substantial advances in the field of preschool mental health. Previously regarded as something of a special-interest discipline holding little interest for mainstream mental health practitioners, early childhood psychopathology has garnered much more attention in public health, clinical, and neuroscience circles. In part, this arises from an accumulating body of evidence demonstrating the longitudinal stability of many disorders with onset in the preschool period. Perhaps more important, however, has been the growing literature documenting the changes in neural function and brain development that have been shown to be associated with preschool psychopathology. Based on this, the field of preschool mental health has garnered attention and interest from prevention researchers and those investigating the neurodevelopmental etiologies of adult mental disorders.

One of the most compelling attractions that early childhood mental health holds for many practitioners is the opportunity to intervene during a period of rapid developmental and brain change. Related to this, the central importance of the parent–child relationship during this phase of child development allows the clinician to target parenting practices, in addition to child behavior. These principles are elaborated in the chapters on treatment, a domain in which significant advances have been made. These factors taken together may be one reason behind the principle and emerging supporting empirical evidence suggesting that early interventions are more effective than those implemented later in life. This may be based on increased neuroplasticity early in life, as well as the long-term benefits of changing parental practices that then continue throughout the life of the child. If such a principle can be scientifically proven in specific disorders or related developmental domains, this would become a paradigm shift for the field of mental health more generally. The intriguing chapters on treatment and sensitive periods in this handbook provide emerging evidence in support of such a principle.

Advances in the understanding of brain development early in life, made possible by significant advances in noninvasive tools to measure brain function and structure in very young children (e.g., functional magnetic resonance imaging and evoked response potentials), have catalyzed the field of mental health, providing key insights into the alterations in brain structure and function that underlie many mental disorders. Along this line, new advances in our understanding of early childhood brain development are reviewed in Chapter 2. Neuroimaging tools and methods, many of which are feasible in infants and young children, have also highlighted in more tangible ways why the early identification of mental disorders must not be ignored, because it leaves an indelible mark on the developing child, refuting the old notion that "he or she will grow out of it." These new findings have given new power and momentum to the field of preschool mental health, and the chapters in this handbook underscore these exciting advances.

Another unique aspect of early childhood mental health is the central importance of the psychosocial environment as a critical component of the world of the developing young child. Along this line, Chapter 1 provides a comprehensive and contemporary review of the new social forces that influence the developing young child in the context of our rapidly changing social structure. Related to this, studies of early development have also elucidated the convergence of psychosocial and biological processes, forces that have come together with unique clarity in this field. Early childhood has proven to be a key developmental period in which psychosocial experiences become embedded in the biological substrate of the developing human. In this way, exciting new findings, first established in animal models, about the biological cascade that is set into motion in response to receiving early nurturing from a caregiver have begun to establish that the prior battle lines between the psychosocial and the biological domains are in many areas a false dichotomy. These exciting and humbling findings validate and underscore the essential importance of early experience, and particularly the essential role of the caretaker–child relationship, in growing psychologically and mentally healthy children. In addition, they have established early childhood mental health as a science, and, equally important, a study of the humanities.

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Part I

Developmental Psychopathology of Early-Onset Disorders

Risk and Resilience

1

Sensitive Periods of Development

Implications for Risk and Resilience

Sonya Troller-Renfree
Nathan A. Fox

Scientists, educators, and clinicians have long been interested in the effects of early experience on social, cognitive, and adaptive behavioral development. Neuroscientists have long argued that there are periods across development of the nervous system during which experience-expected environmental stimuli have greatest impact. These periods are referred to as "sensitive periods" and are thought to be integral to physical, social, and cognitive functioning in adulthood.

In this chapter we focus on how sensitive periods may influence development and provide a survey of research on early childhood sensitive periods in cognition, brain development, and social–emotional development. This chapter is divided into two sections. First, we discuss the history, theory, and methodological considerations associated with research in sensitive periods. Second, we use research on early-life deprivation as a model to investigate sensitive periods in child development. Specifically, we concentrate on three domains known to underlie mental health: cognition, neural development, and social–emotional development.

INVESTIGATION AND INTERPRETATION OF SENSITIVE PERIODS

Work in the area of sensitive periods is part of a larger body of research on the effects of early experience on neural and behavioral development. For many

years, scientists have been interested in the effects of early versus later life experiences on the emergence of multiple domains of adaptive behavior. Sensitive periods are one subset of this greater body of work. Scientists focus on the timing of experience and examine whether there is a particular window of time before which certain experiences do not change brain organization and behavior and after which experience may no longer play a significant role in shaping brain and behavior. Some of the earliest work in identifying these windows of opportunity dates back to the 1930s when ethologist Konrad Lorenz (1935) observed that greylag goslings would form a social attachment with the first moving object they encountered after hatching. This attachment was perceptively identical to how goslings would bond to their biological mother and was termed "imprinting," since imprinted goslings would subsequently avoid other moving objects. Lorenz detailed that goslings without exposure to a moving object within the first 48 hours would not form a strong attachment to the first moving object they encountered, and therefore deemed the first 48 hours to be necessary for the formation of this strong maternal-like bond, a "critical period" in gosling development.

Historically, "critical periods" were defined as rigidly demarcated windows of time during which experience provides input that is essential for normative development, and without this input development is irrevocably altered (Hensch, 2005; Knudsen, 2004). However, subsequent experimental work examining Lorenz's work on imprinting (Hess, 1964; Moltz, 1960) as well as human work examining early social deprivation (Clarke & Clarke, 1977; Rutter, 1980), has called into question whether critical periods for environmental experience are as well-defined and irreversible as originally thought, thus necessitating a reconceptualization of how experience impacts development.

"Sensitive periods," in contrast to critical periods, are a limited time window in development during which a system is particularly sensitive to experience (Bornstein, 1989; Hensch, 2005; Knudsen, 2004). Evidence of sensitive periods is found across many fields (e.g., biology, zoology, medicine, ethology). However, over the last few decades, sensitive periods have become an area of particular interest for understanding and investigating human development. Specifically, the concept of sensitive periods may provide one account as to how early experiences (or the lack thereof) have particularly strong effects on brain and behavior later in life (Bornstein, 1987, 1989; Hensch, 2003; Werker & Hensch, 2015; Werker & Tees, 2005; Zeanah, Gunnar, McCall, Kreppner, & Fox, 2011).

What Defines a Sensitive Period?

Although what defines a sensitive period varies across disciplines, there are a number of characteristics that are necessary to deem a phenomenon a "sensitive" period (for reviews, see Bornstein, 1987, 1989; Knudsen, 2004).

Bornstein (1989) indicated that each sensitive period should have a defined "system" that is being altered by a change in sensitivity to environmental

experiences. Changes to this system may be easily observable and assessed (e.g., visual acuity) or a more a more complex and less easily mapped latent construct (e.g., emotion interpretation), but critically these systems should not be entirely under genetic control and therefore must rely on contributions from experience for development (Knudsen, 2004). William Greenough, a neuroscientist, first proposed two processes by which experience affects the brain: experience expectant and experience dependent. "Experience-expectant" processes are those that the emerging neural circuitry "expects" in order to form adaptive systems for behavior. A good example is vision, with particular types of visual experience playing a formative role early in life. "Experience-dependent" processes are those that form the foundation of individual differences in children's learning and development. The formation of neural circuits "depends" on the particular and unique contexts and stimuli that are provided. On the one hand, experience-expectant processes lend themselves easily to thinking about sensitive periods during which these "expected" events are to occur. Experience-dependent processes, on the other hand, may occur across the lifespan. Each system should have an *asymptote* or *direction* of change (i.e., increase or decrease); it has been suggested, however, that direction of change may not be unidirectional and may be mediated by organism-specific characteristics or prior experiences (Boyce & Ellis, 2005). For example, research examining sensitive periods in IQ development has identified periods of environmental sensitivity for two different directions of change: increased IQ (Brant et al., 2013) and decreased IQ (Fox, Almas, Degnan, Nelson, & Zeanah, 2011; van IJzendoorn, Luijk, & Juffer, 2008).

All sensitive periods should have an *onset* or *opening* period when sensitivity to a particular set of experiences begins to increase, a *duration* of increased sensitivity, and an *offset* during which sensitivity declines. While these features are rather straightforward in definition, they may vary widely across systems. For instance, onsets and offsets may be gradual or very sharp. Similarly, onsets and offsets may be defined by chronological age (time since birth) or developmental age (age at which a child functions across domains). Additionally, for an onset to occur, each system must be developed enough to function, plastic enough for changes to occur, and have the ability to be modulated via a *mechanism* or *pathway* (e.g., up-regulation–down-regulation or excitatory–inhibitory; Fagiolini & Hensch, 2000; Hensch, 2003; Knudsen, 2004).

Finally, it is important to consider that sensitive periods may have different degrees of *variability* across both individuals and species (Bornstein, 1987, 1989). Individual and species variation in duration, onset, offset, mechanism, asymptote, and pathway can make sensitive periods difficult to operationalize and measure. Investigations of variability in sensitive periods are of great interest to many, since they may infer possible areas of most optimal intervention.

Outcomes of a sensitive period affect the system in a number of different ways and include introducing a new function, altering an existing function, or

maintaining an already existing function. Outcomes can have different temporal profiles, ranging from instant to emerging decades later (a "sleeper" effect), and can be short-lived or persist across the lifespan. Finally, some outcomes may be alterable by experiences outside of the sensitive period, whereas others are more permanent.

Examples of Sensitive Periods

One of the clearest and translational studies of sensitive periods comes from the experimental work of Hubel and Wiesel (1959, 1962, 1965; Wiesel & Hubel, 1963) detailing the development of the visual system. Hubel and Wiesel's work documented that when kittens are first born they show a pattern of nonspecialized neural architecture in an area of the brain integral to vision (striate cortex). However, over time, kittens with normal visual development begin to show a highly specialized neural architecture with alternating, columnar connectivity for each eye. Given that this neural specialization begins only after kittens are exposed to a complex visual environment, it was hypothesized that a sensitive period for visual development may exist. To test this hypothesis, Hubel and Wiesel occluded one eye shortly after birth and found that after a short period of time, the occluded eye becomes functionally blind and that the specialized neural representation for the eye never developed. Hubel and Weisel (1963) also demonstrated that if an eye remained occluded for an extended period, then the kitten did not recover normal vision or neuronal specialization in visual cortex. While parallel work obviously cannot be done in humans for ethical reasons, a natural experiment exists in children who are born with congenital cataracts. Consistent with the work Hubel and Weisel, children who have congenital cataracts show altered perceptual development and amorphic development of visual cortex (Lewis, Maurer, & Brent, 1995; Lewis & Maurer, 2005). Furthermore, the study of children with cataracts (binocular and monocular) and amblyopia (poor visual in a single eye due to altered brain circuitry) has identified multiple sensitive periods related to visual acuity, peripheral vision, and detection of global motion (Berardi, Pizzorusso, & Maffei, 2000; Hensch, 2005; Lewis et al., 1995; Lewis & Maurer, 2005).

While development of the visual system shows strong evidence of sensitive periods, it is important to note that a wide variety of systems in human development show similar indications of sensitive periods. Language development has been shown to have many overlapping and interacting sensitive periods during development that lead to optimal language processing (Werker & Hensch, 2015; Werker & Tees, 2005). For instance, within speech perception, separate and cascading sensitive periods appear to exist for phonetic, phonological, lexical, and reading development. Similarly, there is evidence for sensitive periods in face processing. A number of researchers have documented changes in the perception of faces and face-voice integration across the first year, with decreased discrimination across categorical boundaries with

age, a phenomenon known as "perceptual narrowing" (Nelson, 2001). Beginning in the first period of life, one or more sensitive periods appear to exist for the memory of faces, race processing, gender processing, and species processing. The evidence of experience-expectant periods of development within language development and face processing provide two additional examples of sensitive periods in human development, with more examples existing across other domains. They also emphasize that within each domain there are multiple sensitive periods corresponding to the emergence of component processes involved in these complex skills.

Sensitive Periods in Human Development

While there are many well-defined sensitive periods in sensation and perception in both animal and human work, sensitive periods for more complex skills (e.g., cognition or social behaviors) are much harder to investigate for at least two reasons. First, many complex processes have a protracted period of development and rely on the development of a number of integral underlying skills. For instance, intelligence heavily relies on the development of language, executive functions, fluid cognition, and crystallized cognition. In addition to relying on many individual skills, sensitive periods in complex social skills are hard to identify, since it is difficult to delineate typical versus atypical development given the wide variation in onset and presentation of social behavior across contexts and cultures. Second, there are significant ethical considerations associated with investigations of sensitive periods in humans. While animal research allows for carefully controlled and manipulated studies that substantially alter an organism's environment (e.g., severe deprivation, knockout animals), such manipulations commonly produce long-lasting changes that would be unethical in human populations. Given these limitations, much of the research detailing sensitive periods in human development relies on so-called experiments of nature in which environmental manipulations are the result of some societal, social, medical, or genetic perturbation.

One framework that is well suited for the investigation of sensitive periods in humans is found in populations that experience early deprivation. By examining the onset, duration, and extremity of early deprivation, scientists can begin to understand what periods of childhood are critical for neural, cognitive, and social development. There are many different types of early deprivation a child can experience, such as poverty, maltreatment, and neglect, each of which is accompanied by its own constellation of environmental experiences (for review, see Sheridan & McLaughlin, 2014). One major difficulty associated with using deprivation studies to examine sensitive periods is that, for many children, deprivation is long-lasting and it is therefore difficult to parse whether environmental deprivation differentially impacts development at separate points in development. One area of deprivation research with rather abrupt changes in environmental conditions that can begin to untangle

whether environmental deprivation may differentially influence development is the institutional care and international adoption literature. For the remainder of this chapter we summarize current findings that suggest sensitive periods exist for neural, cognitive, and social development, as evidenced by studies of institutional care.

Sensitive Periods in Child Development: Evidence from Studies of Institutional Care

Current estimates suggest that, worldwide, about 8 million children reside in institutional care (United Nation's Children's Fund, 2004, 2007). Children in institutional care experience adverse early experiences that influence a number of domains, including language, cognition, emotion, and attachment/social development.

While early deprivation is a useful model for identifying sensitive periods in human development, there are some important caveats that should be acknowledged. First, alterations in complex behaviors are likely to be distal outcomes of many overlapping and interacting sensitive periods in human development (Knudsen, 2004). Additionally, complex skills tend to comprise more simple subskills (which are likely to have their own individual sensitive periods and developmental cascades) that interact and rely on one another, which makes the assessment of sensitive periods very difficult (Werker & Tees, 2005). Furthermore, evolution and human development rely on multiple mechanisms that compensate for deviations in development. As such, many of the effects discussed in the following sections are likely to be conservative estimates of the effects of early sensitive periods on subsequent functioning (Zeanah et al., 2011).

In contrast to much of the work on sensitive periods in animals and sensory domains in humans, sensitive periods of complex systems in human development are methodologically more difficult to identify. As discussed previously, ethical concern over scientifically manipulating a child's environment is one of the major reasons that it is difficult to identify sensitive periods in human development. Second, many studies examining sensitive periods in human development via natural experiments do not have high degrees of control (i.e., children who are adopted from institutions may be different from those who are not) or a high degree of temporal resolution (i.e., children are more likely to be adopted in early vs. late childhood). Given these constraints, we have outlined how we identified particular components of sensitive periods in the early deprivation literature in Table 1.1.

Postinstitutionalization adoption studies allow investigation of sensitive periods in a number of ways. Children who are exposed to institutionalized care early in life and then placed in high-quality environments (adoptive homes) provide three kinds of evidence for sensitive periods in early childhood. First, extended follow-up of such children allows examination of deficits they may have at the time of adoption and also those that may emerge

TABLE 1.1. Components of Sensitive Periods in the Context of Early Deprivation

Sensitive period component	Definition	Example from early deprivation model
Asymptote	Direction of effects	Does deprivation cause development to be stunted or accelerated?
Onset	Environmental sensitivity is increased	Do children removed from deprivation before a certain age not see deficits?
Offset	Environmental sensitivity is decreased	Is there a point at which continued institutional care does not have a differential effect on development?
Variability	Differences in systems and outcomes between children	Do children with similar caregiving backgrounds show a wide array of performance?
Outcomes	Changes in the individual as a result of sensitive periods	Are children who had early deprivation at increased risk for a negative outcome?

over time. Deficits noted at the time a child is taken out of an institution and placed into care may suggest that the experiences in institutional care are associated with these deficits. This, of course, assumes that no preexisting condition contributed to these deficits. As well, variation in the age at which a child is removed from the institution may help inform whether there are sensitive periods involved in the effects of such early depriving experience. For example, if one child is removed from an institution prior to 6 months of age and another is removed a year later, differences in deficits may suggest that the timing, length of deprivation, or the age of exposure (or all three) contributed to these different outcomes. Again, this assumes that there were no preexisting differences between these two children. Second, improvement or amelioration of deficits after a child is removed from institutional care suggests that the system impacted the child during a sensitive period may be plastic, or that the timing of intervention occurred during the sensitive period (had not reached its offset), or that multiple sensitive periods may exist, or that there is no sensitive period.

Many studies have assessed the effects of institutionalized care on internationally adopted children; however, one seminal cohort worth mentioning is the English and Romanian Adoptees (ERA) Study (Rutter & ERA Study Team, 1998; Rutter, Sonuga-Barke, & Castle, 2010). The ERA Study began in the 1990s and was designed to examine the effects of early deprivation on child development. The sample was drawn from 324 children who were adopted into families in England before 42 months of age. The final sample consisted of 111 children adopted before 24 months and 54 children adopted between 24 and 42 months of age. Additionally, 52 within-country adoptees were recruited for comparison. Data from the ERA Study have demonstrated

that early adversity affects organismic changes that are difficult to ameliorate and extend beyond just prolonged psychosocial deprivation. These changes are referred to as "biological programming" (Rutter, O'Connor, & ERA Study Team, 2004). Rutter and colleagues have demonstrated that children who experience early deprivation show patterns of cognitive deficits that are consistent with biological programming effects or neurological damage. Further evidence of biological programming comes from data detailing increased incidence of disinhibited attachment. Specifically, findings indicate that children who were institutionally deprived are more likely to show disinhibited attachment styles and that there is a relation between disinhibited attachment and duration of deprivation; furthermore, these patterns persist after the restoration of normative family rearing. Data from the ERA study have demonstrated the biological programming effects of early deprivation and suggested sensitive periods in child development across a number of domains (Rutter et al., 2010).

To date, there has been only one randomized controlled study of institutionalized care and early intervention, the Bucharest Early Intervention Project (BEIP). The BEIP randomly assigned young children residing in institutional care in Bucharest, Romania, to either remain in institutionalized care and continue to receive care as usual, as provided by the Romanian Government, or to receive a high-quality foster care intervention (see Zeanah et al., 2003, for more information on study design). Data from the BEIP provide evidence for the effects of early deprivation and allow inspection of the presence of sensitive periods in development by examining the age at which children were removed from the institution and placed into foster care. Continued follow-up of both groups of children (care as usual and foster care) provide evidence of how continued deprivation affects systems of interest.

For the remainder of the chapter we review the evidence of sensitive periods in neural development, cognitive development, attachment, and mental health through the lens of early deprivation.

Sensitive Periods in Neural Development

Sensitive periods in neural development are of great interest given that an understanding of aberrations in neural development may elucidate possible mechanisms associated with more complex cognitive changes, such as the differences seen in IQ and executive functioning (Nelson, Bos, Gunnar, & Sonuga-Barke, 2011). Research findings on the effects of adverse early experiences on neural development generally focus on structural, functional, or a combination of structural and functional neural changes. Structural changes are physical changes to the brain, such as increased or decreased volume, thought to reflect in part the growth of neurons or changes in diffusivity of water molecules in the brain (indicated by diffusion tensor magnetic resonance imaging) thought to reflect the integrity of white-matter tracts or myelin. Functional changes, on the other hand, reflect differential patterns of brain activity or changes in

circuit connectivity reflecting a pattern of use. In the following two sections we review the evidence for sensitive periods in structural and functional brain development. While we review these two bodies of literature separately, it is important to remember that structure and function are linked, given that the use (or lack of use) of brain regions commonly leads to changes in structure. However, how function and structure interact throughout development remains empirically understudied.

Structural Differences

Structural brain development begins a few weeks after conception and continues into the second and third decades of life. Given the protracted time course of neural development, early experiences may influence development starting in the prenatal period. Neural development in the postnatal early infancy period is commonly a period of robust "synaptogenesis" (creation of brain cells), with an abundance of dendrites and axons being produced (Huttenlocher & Dabholkar, 1997). While some evidence suggests that synaptogenesis rates are experience-dependent and vary by region, with more rudimentary areas of the brain typically peaking in cell count before areas that support more complex functions (Huttenlocher & Dabholkar, 1997), other data suggest this may not be the case. For instance, studies in primates have shown that synaptogenesis occurs synchronously across all cortical areas (rather than in a pronounced order) and is independent of environmental input (Rakic, Bourgeois, & Goldman-Rakic, 1994). Following a period in the postnatal months of rapid synaptogenesis, brain regions begin experience-dependent pruning (the removal of synapses, axons, dendrites, etc.) that enables the brain to adapt and organize itself optimally based on environmental demands. Rates of synaptic pruning vary as a function of a hierarchy of circuits, with simple areas/circuits (i.e., visual and motor systems) pruning earlier and faster than more complex areas/circuits (i.e., prefrontal and limbic systems). Another aspect of neural development is "myelination," which is the process of forming a fatty sheath around the axons of neurons that aids in neuronal conduction, speed, and communication. Myelination begins in midinfancy and persists into early and midadulthood, with more complex brain structures completing myelination later than more basic structures (Benes, Turtle, Khan, & Farol, 1994; Yakovlev & LeCours, 1967).

There is much evidence that the presence of expectable, contingent caregiving early in life is essential for proper structural brain development (Sheridan, Fox, Zeanah, McLaughlin, & Nelson, 2012; Tottenham & Sheridan, 2010; Tottenham, 2012a, 2012b). Given that deprivation is associated with the absence of essential environmental experiences, the effects of deprivation on the brain tend to be robust and, in some cases, long-lasting. Here we review the major findings related to volumetric differences, amygdala development, and frontal circuitry; however, there are many other areas of the brain influenced by early deprivation (for review, see Bick & Nelson, 2016).

SENSITIVE PERIODS AND BRAIN VOLUME

Volumetric measures of brain development index, among other things, the efficiency of synaptogenesis, synaptic pruning, and myelination in the whole brain and in specific brain regions. Simply, volumetric measures usually consist of three measures: total volume, white matter volume, and grey matter volume. White matter volume is predominantly composed of myelin and glial cells, and is associated with neuronal communication and connectivity, whereas grey matter is composed of neuronal cell bodies, dendrites, and unmyelinated axons, and is associated with sensory and cognitive processing (Miller, Alston, & Corsellis, 1980; Wilke, Krägeloh-Mann, & Holland, 2007). There is converging evidence that early deprivation is associated with reductions in head size and whole-brain volume, as well as alterations in grey matter and white matter, which suggests there may be many sensitive periods for synaptogenesis, synaptic pruning, and myelin creation early in infancy and early childhood (Hanson et al., 2015; Mehta et al., 2009; Sheridan et al., 2012). Data from the BEIP indicate that early intervention may buffer against the negative effects of early deprivation on white matter but not grey matter development (Sheridan et al., 2012). These findings suggest that there may be separate sensitive periods for white and grey matter development, with the white matter sensitive period lasting longer, occurring later, or being more malleable than the sensitive period for grey matter.

EVIDENCE FOR SENSITIVE PERIODS IN THE AMYGDALA

The limbic system consists of a number of brain structures associated with emotion processing and regulation, memory, motivation, and learning (LeDoux & Phelps, 2010; Mega, Cummings, Salloway, & Malloy, 1997). The amygdala, an area essential for emotion and threat processing, appears to be influenced by institutional care; however, the asymptote (direction of change) may be influenced by a number of contextual factors (Callaghan & Tottenham, 2016). For instance, two postinstitutionalization adoption studies found evidence that early institutional care is associated with increased amygdala volume and a positive relation between amygdala volume and length of time spent in the institution (Mehta et al., 2009; Tottenham et al., 2010). Conversely, another postinstitutionalization adoption study found decreased amygdala volume in children who experienced early deprivation, with a negative relation between amygdala volume and cumulative life stressors (Hanson et al., 2015). Recent work by Tottenham (Callaghan & Tottenham, 2016; Gabard-Durnam et al., 2014; Gee et al., 2013) suggests that both amygdala functioning and connectivity between amygdala and cortical regions change across typical development and are also influenced by adverse experiences. In a series of studies, Tottenham found that children experiencing early adversity displayed more "mature" patterns of amygdala reactivity (similar to older children and adults), as well as more "mature" connectivity. One possibility is that early adverse experience speeds up the development of these connections so as to enhance possibilities

for survival in a stressful environment (Callaghan & Tottenham, 2016). These findings suggest there may be sensitive periods for amygdala development early in life; however, the asymptote may vary substantially based on postinstitution environmental input and individual factors.

EVIDENCE OF SENSITIVE PERIODS IN FRONTAL CIRCUITRY

The prefrontal cortex (PFC) is implicated in a number of complex emotional and cognitive functions, such as executive functions, top-down attentional processes, and self-regulation. The PFC has one of the most protracted developmental time courses in the brain, which makes it highly susceptible to environmental influences such as stress (Arnsten, 2009; Gogtay et al., 2004; Kolb et al., 2012). To date, only two studies have reported an effect of institutional care on PFC development (Hodel et al., 2015; McLaughlin et al., 2014). Both studies found that the PFC was negatively impacted by institutional care (decreased cortical surface area or thickness). While the effects of institutionalized care on specific subregions of the PFC differed slightly across the two studies, these changes do suggest that the PFC may be particularly sensitive to environmental experiences, and that there may be a sensitive period for normative PFC development in the first few years of life.

Resting-State Functional Differences

Sensitive periods related to function while the brain is at rest have received much less attention than structural differences. To date, two studies have looked at functional connectivity in previously institutionalized children using two different neuroimaging methods: positron emission tomography (PET) and functional magnetic resonance imaging (fMRI). Using PET to examine brain glucose metabolism, data indicate that previously institutionalized children show bilateral reductions in metabolic rates in the in the orbitofrontal gyrus, the infralimbic PFC, the medial temporal structures (amygdala and head of hippocampus), the lateral temporal cortex, and the brain stem (Chugani et al., 2001). These data suggest that many of the cognitive and mental health deficits we discuss later in this chapter may be mediated by dysfunction in these brain regions caused by early deprivation (Chugani et al., 2001). Additional evidence for functional differences is found in ventromedial PFC and amygdala connectivity. During typical development, the amygdala and PFC show a period of positive coupling early in life, followed by a period of negative coupling later in development (Callaghan & Tottenham, 2016). However, data from previously institutionalized children indicated more mature patterns of connectivity (negative connectivity) between the ventromedial PFC and amygdala early in life (Gee et al., 2013). These data suggest there may be a period for neural connectivity in circuits related to fear learning that is particularly sensitive to and accelerated by early life stress. To date, no studies have used PET or fMRI in a randomized controlled design, a necessary scientific step to test the presence of sensitive periods in brain development.

Additional evidence for sensitive periods in functional brain activity comes from studies using electroencephalography (EEG). A series of studies from the BEIP at child ages 30 months, 42 months, and 8 years have documented both the negative effect of early deprivation on neural activity, as well as the possible amelioration of these deficits with early intervention. Prior to the implementation of the BEIP intervention, when participants were 30 months of age, early neglect was related to more immature patterns of brain activity—higher levels of lower-frequency activity (theta oscillations) and lower levels of higher-frequency brain activity (alpha and beta oscillations)—when compared to community controls (Marshall & Fox, 2004). This pattern of results remained significant at 42 months and at 8 years of age for children randomized to remain in institutional care; however, a different pattern of activation emerged for children who were randomized to receive a high-quality caregiving intervention (Marshall, Reeb, Fox, Nelson, & Zeanah, 2008; Vanderwert, Marshall, Nelson, Zeanah, & Fox, 2010). At age 8, children who were removed from institutional care and placed into a therapeutic foster care setting began to show more developmentally typical patterns of neural activity (Vanderwert et al., 2010). However, these intervention effects were qualified by the age at which children were placed into foster care. By age 8, children placed into foster care before 24 months showed neural activity indistinguishable from that of never-institutionalized community controls, while children placed after 24 months of age showed activation similar to that of children randomized to remain in institutionalized care. These findings have two major implications for understanding sensitive periods in specific aspects of brain development. First, it appears that early deprivation has noticeable effects on EEG activity by 30 months of age, suggesting that the onset of sensitive periods related to neural activity begin early in life. Second, aberrations in neural activity related to early deprivation may be ameliorated with intervention at or before 2 years of age. However, given that children who received intervention after 2 years of age did not show intervention effects, it is possible that one or more sensitive periods related to neural activity may close as early as 2 years of age. Furthermore, given that children who received the foster care intervention before 24 months of age did not show improved patterns of neural activity at 30 months of age, and that these effects were only evident later in development, it is important to consider that amelioration of early deficits may rely on long-lasting environmental interventions or that outcomes related to early intervention may not appear until later in life (sleeper effect).

Sensitive Periods in Cognitive Development

IQ

IQ is commonly considered a "gold standard" among psychologists as a measure of assessing human intelligence and is heavily relied upon for the

diagnosis of intellectual disabilities. Unlike many cognitive assessments, IQ is commonly standardized, age-adjusted, and thought to remain relatively stable across the lifespan, particularly in adulthood. Methods of IQ assessment vary over the lifespan, but most research is conducted using standardized assessments such as the Wechsler (1974) family of tests, Stanford–Binet (Thorndike, Hagen, & Sattler, 1986), Woodcock–Johnson (Woodcock & Johnson, 1989), and the Bayley (2006) scales for young children.

Evidence from a wide range of studies suggests that early deprivation has marked effects on the development of IQ (Fox et al., 2011; Nelson et al., 2007; Rutter et al., 2010; van IJzendoorn et al., 2008). These studies show that deprivation during early childhood is associated with lower IQ scores.

Studies examining the onset of sensitive periods related to IQ have shown that the earlier children are removed from deprivation, the less likely they are to show reduced IQs. Two studies of early deprivation provide strong evidence for the existence an IQ-related sensitive period. One postinstitutionalization adoption study (Rutter & ERA Study Team, 1998) found that children adopted under the age of 6 months did not show decreased IQ at ages 4–6 or at age 11, but children adopted between 6 and 24 months did show decreased IQ at ages 4–6 and age 11. These results suggest that the onset of an IQ-related sensitive period may begin around 6 months of age, with a duration well into early childhood.

Evidence supporting the existence of sensitive periods in IQ development also comes from the BEIP. Consistent with other studies, children in the BEIP who experienced early psychosocial deprivation showed reduced IQ scores (Smyke et al., 2007). Additionally, children removed from institutional care at younger ages showed smaller decreases in IQ at 42 and 54 months of age, suggesting that sensitive period onset is likely in late infancy or early toddlerhood (Nelson et al., 2007). However, when examining the IQ of children ages 8 and 12, a different pattern begins to emerge, showing fewer differences in IQ, based on timing of placement in foster care (Almas, Degnan, Nelson, Zeanah, & Fox, under review; Fox et al., 2011). Interestingly, these changes appear to be related to environmental experiences following initial randomization, such as reduced time in institutional care, placement into government foster care homes, and stability of home placement, suggesting either that sensitive periods related to IQ may have a long duration (into middle childhood) or that IQ outcomes are alterable by some kinds of environmental experiences following the sensitive period.

Executive Functions

"Executive functioning" is commonly defined as the skillful employment of three cognitive processes—working memory, inhibitory control, and attention shifting—in order to complete a goal. Executive skills are thought to be highly susceptible to environmental influences given that they have a protracted development across childhood and have been linked to a variety of outcomes

in adulthood, such as academic achievement, incarceration, substance abuse, and overall physical and mental health (Moffitt et al., 2011). While executive functioning is essential for the assessment of IQ, studies have shown that IQ assessments do a poor job of evaluating executive functioning, and that IQ and executive functions are separable constructs (Ardila, Pineda, & Rosselli, 2000).

Similar to IQ, executive functions appear to be negatively impacted by early deprivation; however, findings vary by assessment method, age of assessment, and specific executive skill (Hostinar, Stellern, Schaefer, Carlson, & Gunnar, 2012; McDermott et al., 2013; Merz & McCall, 2011; Pollak et al., 2010). Merz and McCall (2011) found that children adopted from institutionalized care were more likely to exhibit executive function deficits. Additionally, they found that children adopted after 18 months fared worse than those adopted before 18 months, suggesting that the onset for sensitive periods related to executive functions may be within the first year of life.

Further evidence of sensitive periods in executive development comes from two studies that utilized the Cambridge Neuropsychological Test and Automated Battery (CANTAB; Cambridge Cognition, Cambridge, UK) to assess executive skills in institutionalized and previously institutionalized children at 8 years of age (Bos, Fox, Zeanah, & Nelson, 2009; Pollak et al., 2010). Pollak and colleagues found that postinstitutionalized children adopted at or after 12 months of age showed deficits in the spatial working memory and paired associated learning task, while children adopted out of institutionalized care at or before 8 months of age did not show these deficits when compared to a nonadopted comparison group. Similarly, studies from the BEIP showed children with a history of institutional care preformed worse on visual memory and executive functioning (ages 8 and 12) and learning (age 12) when compared to noninstitutionalized peers (Bick, Zeanah, Fox, & Nelson, under review; Bos et al., 2009). Additionally, early removal from institutional care was also not associated with improved memory and executive skills. Furthermore, this pattern of data may also suggest that, at least for some forms of executive function, there may be a sensitive period in infancy, with deficits difficult to remediate later in life.

Other studies examining executive functions of children who have experienced institutionalized care also show evidence of deficits when examining both behavioral and neural correlates of executive functions. One task commonly used to assess attention, inhibitory control, and error monitoring is the Go/No-go task. Data from the BEIP show that children in institutionalized care show both behavioral and neural deficits on the Go/No-go and Flanker tasks (Loman et al., 2013; McDermott, Westerlund, Zeanah, Nelson, & Fox, 2012). In a Flanker task, participants are instructed to identify the direction of a center arrow, which is surrounded by four flanking arrows that can point in the same direction or in the opposite direction of the center arrow (<<<<< or <<><<). The flanker task is thought to index conflict monitoring, selective

attention, and inhibitory control. Specifically, on the Go/No-go task, children who were randomized to remain in institutionalized care showed reduced behavioral performance (accuracy and reaction time), as well as perturbed neural correlates associated with reduced attentional processing of No-go cues and poor detection of errors, while children removed from institutional care and placed in high-quality foster care only showed reduced attentional processing of No-go cues (McDermott et al., 2012). Similarly, a separate study of postinstitutionalized adopted children showed reduced behavioral performance in previously institutionalized children; however, neural correlates of attentional processing and error detection were not consistent with the findings from BEIP (Loman et al., 2013).

Another task commonly used to assess behavioral and neural correlates of executive function is the Flanker task. Similar to the Go/No-go task, the Flanker task was administered to both the BEIP sample and a postinstitutionalized sample (Loman et al., 2013; McDermott et al., 2013). In the BEIP sample, children randomized to remain in institutionalized care showed that early psychosocial deprivation was associated with impaired inhibitory control (measured behaviorally), as well as perturbed neural correlates of response monitoring (McDermott et al., 2013). Children who received the foster care intervention exhibited better response monitoring when compared to children who remained in institutional care. Furthermore, children within the foster care group who exhibited larger neural correlates associated with error monitoring exhibited less behavioral problems, indicating that executive functions may be an important component of healthy social–emotional development. Similarly, a separate sample of postinstitutionalized children adopted into the United States showed deficits in inhibitory control, with evidence that children adopted later exhibited larger deficits (Loman et al., 2013). Furthermore, postinstitutionalized adoptees showed altered neural correlates associated with error and response monitoring.

Together these findings suggest that children who experience early deprivation show behavioral problems and some neural evidence of reduction in inhibitory skills, providing further evidence for sensitive periods for executive development early in life. However, given that children who experienced prolonged institutional care showed worse deficits than those removed from institutional care on a number of measures, it is possible that the sensitive period for executive development may extend into middle childhood or that many sensitive periods for executive development may exist.

Sensitive Periods in Social and Emotional Development

The absence of consistent, contingent caregiving in institutional care has made children reared in this setting the focus of attachment research for decades. Across many studies it has been demonstrated that institutional care is related to abnormal patterns of attachment, with reduced security and increased

prevalence of atypical attachment patterns (Steele, Steele, Jin, Archer, & Herreros, 2009; Vorria et al., 2003; Zeanah, Smyke, Koga, & Carlson, 2005). A meta-analysis examining whether removal from institutional care facilitates more normative patterns of attachment found that children adopted before age 12 months were more likely to be securely attached than those adopted after (van den Dries, Juffer, van IJzendoorn, & Bakermans-Kranenburg, 2009). Data from the BEIP also suggest that removal from institutional care and placement into foster care reduces insecure atypical attachment patterns and increases secure attachment (Smyke, Zeanah, Fox, Nelson, & Guthrie, 2010). These findings all suggest that a sensitive period for attachment exists early in development. During this sensitive period, the presence of a high-quality, consistent caregiver appears to be essential for the formation of secure bonds. These data also suggest that this sensitive period for attachment may open near the end of the first year of life, as evidenced by the meta-analysis of prior postinstitutionalized attachment studies.

Children in institutionalized care also show "indiscriminate friendliness," which is defined as disinhibited affectionate and friendly behavior towards all adults (including strangers) without fear (Tizard, 1977). Indiscriminate friendliness has been considered by some to be another variety of attachment disorder (O'Connor, Rutter, & ERA Study Team, 2000), whereas others believe it is an independent symptom (e.g., Zeanah, Smyke, & Dumitrescu, 2002). One of the first studies of indiscriminate behavior in institutionalized children revealed that almost 40% of children in institutionalized care exhibited indiscriminate behavior by age 4 (Tizard & Rees, 1975). Further studies of postinstitutionalized adoptees show similar patterns of increased indiscriminate behavior to that in children who were previously institutionalized (Hodges & Tizard, 1989; Rutter et al., 2007). Rutter and colleagues also demonstrated that children who were institutionalized beyond the age of 6 months were more likely to show indiscriminate friendliness, and they suggested that experience-based biological programming after 6 months of age may lead to indiscriminate behaviors. Consistent with other samples, children in the BEIP showed higher levels of indiscriminate friendliness (Zeanah et al., 2002); however, children who were identified as favorites of caregivers showed lower levels of indiscriminate behavior. Interestingly, children randomized to the foster care intervention showed similar levels of indiscriminate friendliness to that of children randomized to remain in institutional care. These findings suggest that there may be a sensitive period for indiscriminate social behavior that begins after 6 months of age. Furthermore, as evidenced by less indiscriminate behavior in children who were favorites of the institutional staff, the presence of an attached and attentive caregiver may be the expected environmental input (experience-expectant) for this sensitive period. Furthermore, given that later interventions (e.g., BEIP foster care, which began at a mean age of 22 months) did not reduce indiscriminate behavior, it is probable that the sensitive period for indiscriminate behavior may close by the second year of life.

Sensitive Periods in Mental Health

The final area of development we review for evidence of sensitive periods is mental health. One of the difficulties with identifying sensitive periods in mental health is that psychopathology is commonly considered an outcome that is measured sometimes years after the sensitive period may have occurred. Similarly, given that many psychiatric disorders do not appear until later childhood and early adolescence, it has been postulated that mental health problems may be a sleeper effect, reflective of the presence or lack of specific experiences in infancy and early childhood (Pine & Fox, 2015).

For over 50 years, it has been known that children who experience early deprivation are at increased risk for developing psychiatric disorders (Bos et al., 2011; Widom, DuMont, & Czaja, 2007). Psychopathology rates among previously institutionalized children are elevated across both internalizing and externalizing domains, with particularly high rates of attention problems, hyperactivity, poor self-regulation, attachment disorders, and anxiety (Colvert et al., 2008; Ellis, Fisher, & Zaharie, 2004; MacLean, 2003; Tizard & Rees, 1975).

Many researchers have examined the psychiatric consequences of early deprivation; however, a series of studies from the BEIP project provides a comprehensive view of both the effects of early deprivation and early intervention. The first standardized assessment of mental health in the BEIP sample, conducted at 54 months of age, found that early deprivation was associated with a higher likelihood for both externalizing and internalizing disorders (Zeanah et al., 2009). Children who received the foster care intervention were less likely to have internalizing disorders (primarily anxiety) but were equally likely to exhibit externalizing disorder. At age 12, psychiatric disorders were reassessed and, consistent with the 54-month findings, results indicated that children who experienced early deprivation were still at elevated risk for both internalizing and externalizing disorders (Humphreys, Gleason, et al., 2015). However, inconsistent with the findings at 54 months, children who received the foster care intervention were less likely to exhibit externalizing disorders but equally as likely to exhibit internalizing disorders as children randomized to remain in institutional care. Importantly, additional analyses revealed that children in the foster care intervention who had stable foster care placements showed less internalizing and externalizing symptoms than foster care children who had disrupted foster care placements. Another study from the BEIP also found that callous and unemotional traits, which are strongly related to psychopathology, were significantly higher in children who had experienced institutionalized care (Humphreys, McGoron, et al., 2015). This study also found that the BEIP foster care intervention decreased the number of callous unemotional traits in boys, with caregiver responsiveness moderating this relation. Consistent with the large body of literature detailing the negative effects of institutionalized care, findings from the BEIP project suggest that a sensitive period related to the development of internalizing and externalizing

disorders may exist within the first 3 years of life. Critically, mental health outcomes associated with these early-life sensitive periods may be influenced by a number of environmental factors, such as removal from institutional care, caregiver responsiveness, and consistent caregiving placement.

CONCLUSIONS

Contemporary research on sensitive periods provides us with a framework for pinpointing the effects of early experience on adaptive and maladaptive behavior and therefore risk for mental disorders. Identification of sensitive periods, and the mechanisms and pathways that underlie them, may provide information for the design of targeted treatments and preventive interventions and inform us of the developmental ages at which such interventions may be most effective. Furthermore, while most of the examples provided in this chapter have focused on sensitive periods for maladaptive behaviors, it is important to note that there is evidence for sensitive periods for expertise and skills development as well. For instance, one recent study has demonstrated that individuals with higher intelligence show a pattern of prolonged environmental sensitivity to enhance learning, and related to IQ, suggesting that they may have an extended sensitive period for intellectual development (Brant et al., 2013). Finally, emerging research indicates that sensitive periods may be able to be reopened—particularly via pharmacological interventions (Gervain et al., 2013; Hensch & Bilimoria, 2012).

In this chapter we have used early deprivation, specifically, institutional care, as a model with which to investigate sensitive periods in neural, cognitive, and social–emotional development. Currently there are many lines of research investigating sensitive periods that use a multitude of models and systems, all of which highlight the importance of integral environmental experiences during heightened periods of sensitivity in development. Whereas we have encouraged the reader to consider how sensitive periods in child development may play a role in development, as well as risk and early intervention during the preschool years, the following chapters in this volume discuss the development of social and mental health.

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2

Effects of Early Environment and Caregiving

Risk and Protective Factors in Developmental Psychopathology

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There is a large body of literature on the importance of the early years of life for future health, development, and well-being in childhood, adolescence, and the adult years (Anderson, 2002; National Research Council and Institute of Medicine, 2000; Perry, 2002; Shonkoff et al., 2012; Sroufe, Byron, & Kreutzer, 1990; Zigler & Berman, 1983). These years are characterized by rapid, complex, and profound developmental changes, possibly representing a sensitive period during which experiences may either promote or hinder a child's optimal development. In the course of their first 5 years, young children form mental representations of their psychological, social, and physical realms, and develop hypotheses about their worlds using interactions to test and refine these hypotheses (Lieberman & Van Horn, 2008). Therefore, exposure to risk is integral to how a child understands the world, develops an internal working model of the self and relationships, and acquires a coping repertoire. In addition, emerging research in the field of developmental neuroscience suggests that stress in early life negatively impacts aspects of brain and physical development, and is associated with structural and functional alterations in specific brain regions (Kaufman, Plotsky, Nemeroff, & Charney,

2000; Nelson & Carver, 1998). During this period of vulnerability, a host of environmental risk factors has been identified as compromising children's development and subsequent developmental trajectory.

Social ecology is a useful model in understanding the complexity of factors introduced in a child's early environment. Based on the work of developmental psychologist Urie Bronfenbrenner (1979), social ecology maps environmental systems at varying levels of distance from a child (e.g., family, home, school, community, and society) and provides a framework for understanding the relationships among these systems (Kazak, Rourke, & Navsaria, 2009). In considering these environmental systems through the lens of developmental psychopathology, both healthy and pathological development result from a continuous interplay of interactions between a child and the active environmental systems in which he or she functions. While adverse outcomes are associated with risk factors, some children exhibit resilience and do not experience such outcomes. "Resilience" is defined as a developmental process that occurs in the face of significant adversity or risk, encompassing positive adaptation and producing healthy outcomes (Deater-Deckard, Ivy, & Smith, 2005; Luthar, Cicchetti, & Becker, 2000). The factors that lead to healthy outcomes in these contexts are labeled as "protective factors" (Naglieri & LeBuffe, 2005).

Our goal in this chapter is to review the developmental outcomes associated with several major risk factors present within the various ecological systems in which a child develops. We also highlight protective factors present in the early years that may offset children's risk trajectories. Informed by the social-ecological model, early childhood family and contextual factors are organized around three major areas paralleling Bronfenbrenner's ecological framework for the developing child: (1) parenting characteristics and environment, (2) family structure, and (3) community context. Additionally, we discuss emerging factors in the child's environment that require special attention, including culture, technology, and same-sex couples (see Figure 2.1). For each section, we summarize relevant research on the origins of risk, outcomes, and pathways of risk and protective mechanisms.

PARENTING FACTORS: PARENT CHARACTERISTICS AND PARENTING ENVIRONMENT

The act of parenting represents a convergence of varied influences residing within the parent (e.g., age, experience, stability, early experiences, attributions of the child) and values informed by community and societal expectations. Therefore, a seemingly straightforward interaction between a parent and child actually signifies the complex outcome of numerous multigenerational factors from various environmental systems coming together. These interactions between a parent and child are central to a child's early development for multiple reasons. The parent–child relationship serves as a regulatory

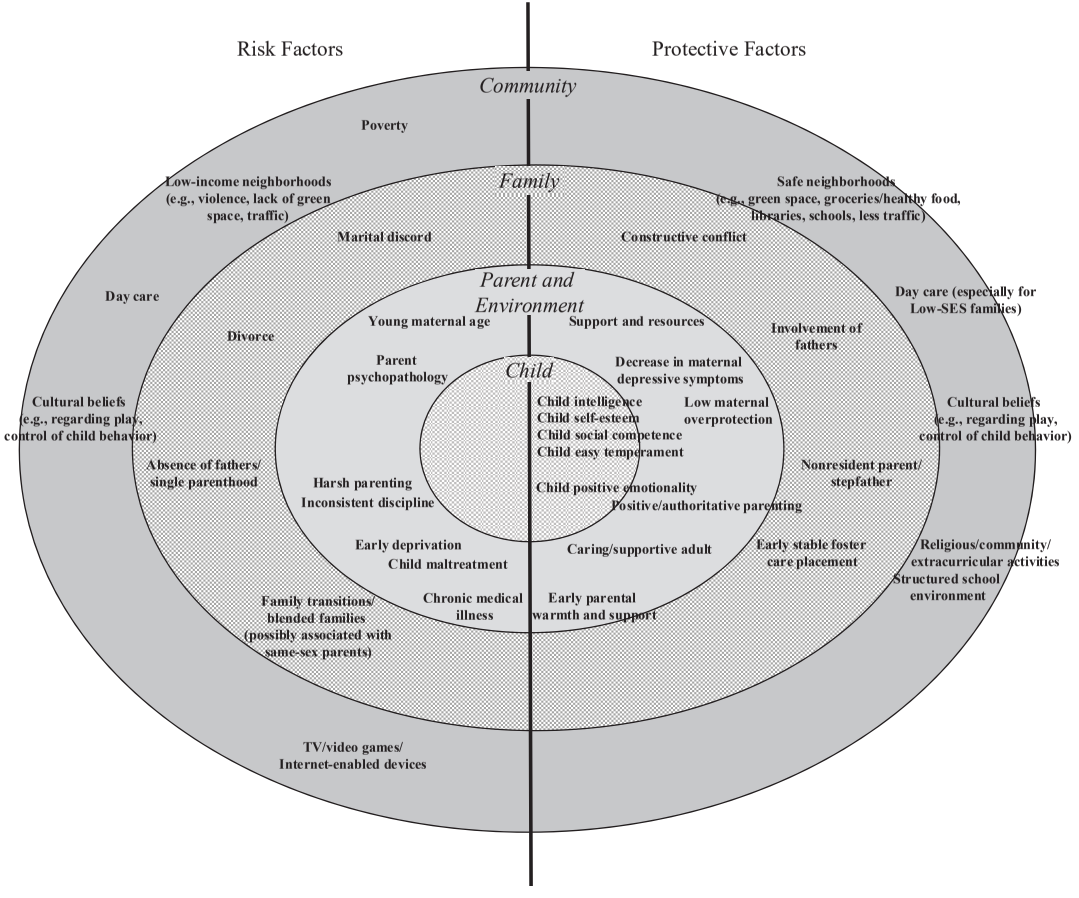

FIGURE 2.1. Risk (left) and protective (right) factors from early environment and caregiving. Associated risk factors are matched with corresponding protective factors horizontally. A color version of this figure is available at *www.guilford.com/p/luby*.

mechanism by which a child develops adaptive emotion regulation patterns and problem-solving skills, and facilitates autonomy development, exploration, and self-control (Dallaire & Weinraub, 2005; Deater-Deckard et al., 2005; Hartup, 1989). Factors that hinder healthy parent–child functioning ultimately produce suboptimal or even detrimental outcomes for a child. In the following section, we present several risk factors specific to parents (e.g., age, mental health, chronic illness), followed by parenting practices (e.g., harsh parenting, inconsistency, deprivation, maltreatment) that profoundly impact children's functioning and development.

Young Parental Age

While the teen birth rate has been steadily declining in the United States over the past decade, it still remains significantly higher than that in most other developed nations (Martin, Hamilton, Osterman, Curtin, & Matthews, 2015), particularly among Hispanic and black adolescents. A number of additional risk factors are associated with teen pregnancy, including low socioeconomic status, poor academic performance, single-mother households, unemployment, and history of child abuse or neglect (Coley & Chase-Lansdale, 1998; Garwood, Gerassi, Jonson-Reid, Plax, & Drake, 2015; Gibb, Fergusson, Horwood, & Boden, 2015). Children born to teen parents are at increased risk for delays in cognitive development, school adjustment problems, and behavior problems such as aggression and impulse control problems (Coley & Chase-Lansdale, 1998; Terry-Humen, Manlove, & Moore, 2005). These findings have not been consistent, however, and some research suggests that risk to offspring of teen parents may be more related to the associated sociodemographic and family risks described earlier than to maternal age (Beers & Hollo, 2009; Hawkes & Joshi, 2012). Less is known about maternal age and risk of specific psychopathology in offspring. For example, depression is common in teen parents, and though it may influence parenting skills, there are few data regarding the effect of maternal age over and above other risk factors (e.g., poverty, single parenthood) in terms of conferring risk to offspring (Goodman et al., 2011).

Parenting is a particular concern among teen parents, because adverse developmental outcomes in offspring can often be attributable to maladaptive parenting practices (Lounds, Borkowski, & Whitman, 2006). A few reports (though not all) have found children of adolescent parents to be at higher risk for abuse and neglect (Afifi, 2007; Beers & Hollo, 2009; Black et al., 2002), as well as exposure to interpersonal violence, which in turn is associated with increased risk for posttraumatic stress disorder (PTSD) in offspring (Enlow, Blood, & Egeland, 2013). Adolescent motherhood is associated with less sensitivity, less verbal interaction, and poorer dyadic interactions with the infant; however, there has been some suggestion that maladaptive parenting continues to worsen as adolescents' children grow older (Coley & Chase-Lansdale, 1998). For example, findings from a large longitudinal study (Fragile Families

and Child Well-Being Study) found adolescent motherhood to be predictive of increased risk for psychological and physical aggression, and spanking from infancy through age 5, even when controlling for commonly co-occurring social and cultural risk factors (Lee, 2009).

It is important to note that not all teen parents are "incompetent," and that there appears to be a continuum of risk especially in terms of age of the teen and amount of sociodemographic risk (Coley & Chase-Lansdale, 1998; Jaffee, Caspi, Moffitt, Belsky, & Silva, 2001; Lewin, Mitchell, & Ronzio, 2013; Roosa & Vaughan, 1984). Some studies suggest that given adequate support and resources, children of adolescent parents do equally as well as children of older parents (Klein, 2005), especially when fathers are more involved (Howard, Lefever, Borkowski, & Whitman, 2006; Lee, 2009). More work is needed to understand better the relationship between young parental age and risk for adverse child outcomes, particularly as it relates to important sociodemographic characteristics. This will help to better inform policy and targeted interventions.

Parental Mental Health

Mental disorders, especially depression and anxiety, are common during the childbearing years and have significant effects on the early environment of young children. Parental psychopathology has been associated with offspring internalizing and externalizing disorders, as well as with behavioral, social, and emotional difficulties more generally (Chronis et al., 2003). Because of young children's intrinsic reliance on their caregivers, early exposure to parental psychopathology may have an even greater effect on child development than later childhood exposure (Goodman & Gotlib, 1999; Goodman et al., 2011). Furthermore, earlier exposures to adversity, such as that associated with parental psychopathology, can start a cascade of adverse developmental pathways (Cicchetti & Curtis, 2006). Thus, understanding the relationships between parental psychopathology and early childhood development are essential for the health and well-being of young children.

Early research regarding the effects of parental psychopathology on offspring development primarily focused on familial transmission of risk for schizophrenia, and found increased rates of mental illness in the children of parents with schizophrenia (Hanson, Gottesman, & Meehl, 1977; Sameroff & Seifer, 1983). Since that time, preschoolers of parents with various psychiatric disorders, such as bipolar and eating disorders have been found to exhibit cognitive, emotional, and social deficits, and to be at a greater risk for psychopathology (e.g., Birmaher et al., 2010; Hirshfeld-Becker et al., 2006; Luby & Navsaria, 2010; Micali, Stahl, Treasure, & Simonoff, 2014).

Most work has focused on parental mood and anxiety disorders, since these disorders are particularly common in parents of childrearing age, with lifetime rates between 10 and 30% (Kessler, 2006; Lyons-Ruth, Wolfe, Lyubchik, & Steingard, 2002). Mounting evidence shows the adverse effects of

depression exposure during pregnancy and early childhood with lasting consequences over and above current parental depressive symptoms (Pawlby, Hay, Sharp, Waters, & O'Keane, 2009; Pearson et al., 2013). For example, Zahn-Waxler, Iannotti, Cummings, and Denham (1990) found that children whose mothers were depressed during pregnancy were more likely to exhibit dysregulated aggression and heightened emotionality at age 4. Others have also found evidence for increased behavior problems, and higher rates of internalizing symptoms in preschool children (Brennan et al., 2000; Marchand & Hock, 1998). Parental depression is associated with not only internalizing and externalizing symptoms but also difficulties with affect regulation (Leve et al., 2010; Maughan, Cicchetti, Toth, & Rogosch, 2007), emotional adjustment (Kerr et al., 2013), social acceptance (Maughan et al., 2007), and cortisol regulation (Laurent et al., 2013) in young children, all of which may be precursors to later psychopathology.

The timing of parental depression appears to be important for child outcomes. A recent meta-analysis concluded that the adverse effects on offspring development associated with depressed mothers were larger when exposure occurred earlier rather than later in childhood. (Goodman et al., 2011). Other studies have examined chronicity and severity of depressive episodes as they relate to child developmental outcomes. In large longitudinal studies, both chronicity (Dannemiller, 1999) and increasing severity (Brennan et al., 2000) of maternal depression were associated with worse cognitive outcomes and increased problematic behavior in preschoolers. Ashman, Dawson, and Panagiotides (2008) also found chronic depression in mothers to be predictive of higher levels of externalizing symptoms and lower levels of social competence in offspring. They also found chronic maternal depression to be related to offspring's decreased generalized brain activation (as measured by electroencephalogram [EEG]) and increased vagal tone, an indicator of decreased emotion regulation and attention (Ashman et al., 2008).

Most research to date has focused on the effects of maternal depression on child outcomes, and little is known about potential differences between maternal and paternal psychopathology. In a meta-analysis, Connell and Goodman (2002) found both maternal and paternal psychopathology to be associated with externalizing disorders in children. Interestingly, maternal psychopathology was most predictive of psychopathology in younger children, while paternal psychopathology was more predictive of psychopathology in older children. In a longitudinal study, Breaux, Harvey, and Lugo-Candelas (2014) found that psychopathology in parents of children age 3 predicted externalizing and internalizing symptoms at age 6. In addition, the father's symptoms were important in predicting offspring symptoms, over and above maternal symptoms. Not surprisingly, children whose parents displayed multiple, co-occurring psychiatric disorders displayed more difficulties. More work in this area is clearly needed and may help to guide prevention and intervention efforts.

Though the relationship between parental psychopathology and adverse child outcomes has been clearly established, the mechanisms by which this occurs are complex and are less understood. Authors of seminal papers

(Goodman & Gotlib, 1999; Sameroff & Seifer, 1983) have proposed several mechanisms, including genetics, dysfunctional neuroregulatory mechanisms, exposure to stressful life events, as well as exposure to negative cognitions, behaviors, and affect of the parent. Although these models were posited specifically for depression, the applicability to psychopathology in general is likely equally valid.

Genetic risk for psychopathology is one mechanism of intergenerational risk transmission. Twin and adoption studies are particularly useful in elucidating gene and environmental effects of parental psychopathology on offspring development. The Early Growth and Development Study (EGDS) is a large, longitudinal study utilizing an adoptive parent (at birth) design to parse out the genetic and environmental contributions of parental psychopathology and environmental risk on children's development and outcomes (Leve et al., 2013). Findings from several recent studies indicate a complex role between genetics and the environment in child outcomes, because both depression in adoptive parents and in birth parents was associated with internalizing and externalizing disorders in children (Kerr et al., 2013; McAdams et al., 2015). Evocative gene–environment relationships were also found, whereby offspring whose birth mothers exhibited externalizing psychopathology were more likely to have adoptive mothers react negatively to child behaviors, especially when the adoptive mothers were experiencing marital distress, which led to the development of subsequent offspring behavior disorder diagnoses (Fearon et al., 2015). However, when the adoptive parents were not under distress, children whose birth mothers had externalizing disorders were the least likely to experience maladaptive parenting, suggesting that child traits evoke poor care only when the family environment is suboptimal.

In addition to genetic effects, parental psychopathology may impact the child's environment early on. Several well-studied environmental influences include social learning, exposure to stressful environments, and parenting practices. For example, maternal depression combined with negative parenting behaviors has been associated with deficits in emotion recognition in preschool children (Kujawa et al., 2014). Furthermore, young children of parents with psychopathology may also be at greater risk for exposure to stressful life events due in part to the "stress generation hypothesis" (Hammen, 1991), which asserts that people experiencing episodes of mental illness, particularly depression, may be more likely to make choices or behave in ways that generate or contribute to stressful events that in turn perpetuate the disorder. Parents with psychopathology may "select" high-stress environments because of family conflict, poor choices or poor problem solving, or downward social drift associated with mental illness.

A large body of research has focused on the effects of parental psychopathology on parenting. In a comprehensive review, Lovejoy, Graczyk, O'Hare, and Neuman (2000) characterized the following parenting features associated with parental depression: increased hostility, less effective communication styles, decreased maternal responsivity to child behavior, and more negative and fewer positive interactions. More specifically, risk seems to be enhanced in

young children of parents with current depression, who may be more likely to be hostile and irritable toward the child. More recent work has suggested that parenting behaviors may change over time in relation to changes in depressive symptoms (Errázuriz Arellano, Harvey, & Thakar, 2012). Parents with schizophrenia display problematic parenting behaviors, such as decreased communication, decreased warmth, decreased supervision, increased hostility, and more overprotection (Malhotra, Kumar, & Verma, 2015). Similarly, anxious parents are thought to exhibit more "anxiety-promoting" behaviors than do nonanxious parents, which may be an important factor in intergenerational risk transmission of anxiety (Budinger, Drazdowski, & Ginsburg, 2013). For example, mothers with increased anxiety show decreased warmth in interaction with their children (Whaley, Pinto, & Sigman, 1999; Woodruff-Borden, Morrow, Bourland, & Cambron, 2002), and anxious parents may also elevate their children's risk appraisal through discussion and catastrophizing cognitions (Moore, Whaley, & Sigman, 2004).

The transactional or reciprocal relationship between children and parents is increasingly recognized as critically important in our understanding of child development. Several recent studies have highlighted the bidirectional influences of maternal depression and young child affective expression (Forbes et al., 2008), preschool externalizing symptoms (Harvey & Metcalfe, 2012), and child internalizing and externalizing disorders (Bagner, Pettit, Lewinsohn, Seeley, & Jaccard, 2013). Reciprocal effects of child behavior and parenting may be particularly salient during early childhood (Harvey & Metcalfe, 2012; Verhoeven, Junger, van Aken, Deković, & van Aken, 2010). Findings from the previously described EGDS study also highlight reciprocal child–parent effects, whereas child externalizing and internalizing behavior was predictive of subsequent adoptive parents' depression (McAdams et al., 2015). In the large, multisite study of antidepressant treatment for adults with depression (STAR*D study), significant decreases in child psychopathology symptoms were found in the year following the mother's remission compared to those in children of mothers who did not remit (Wickramaratne et al., 2011). Children of mothers who did not remit were found to have increasing levels of externalizing symptoms over time (Wickramaratne et al., 2011). While there is some evidence that successful treatment of maternal depression may be related to improvements in child symptoms, the findings are not specific to preschool children. Furthermore, treatment of maternal depression during the postpartum period has not been found to be sufficient to ameliorate risk to infant and toddlers (Clark, Tluczek, & Wenzel, 2003; Forman et al., 2007; Murray, Cooper, Wilson, & Romaniuk, 2003). Thus, further work is needed to determine both the timing and type of interventions (Gunlicks & Weissman, 2008), such as early, preventive, and dyadic (Beardslee, Gladstone, & O'Connor, 2011; Luby, Lenze, & Tillman, 2012).

Few studies have focused on resilience, likely due to the difficulties in interpreting research findings in terms of decreased resilience or increased risk (Reuben & Shaw, 2015). One study found that child intelligence and child social competence were important predictors of resilience in the context of

parental psychopathology (Radke-Yarrow & Sherman, 1990). A more recent study of high-risk offspring of depressed parents found child high self-esteem and easy temperament characteristics to predict absence of diagnosis over time (Lewandowski et al., 2014). Furthermore, consistently high functioning over the study's 20-year follow-up period was associated with offspring self-esteem and low levels of maternal overprotection (Lewandowski et al., 2014). While important, the authors warn that very few offspring met criteria for resilience in this study, which limits firm conclusions. Other studies have suggested that decreases in maternal depressive symptoms are associated with improvements in young children's executive functioning and reductions in problem behaviors (Hughes, Roman, Hart, & Ensor, 2013; Shaw, Connell, Dishion, Wilson, & Gardner, 2009). Other researchers have found that factors thought to be protective are not as powerful in the context of severe depressive symptoms or higher risk contexts (see Lee, Halpern, Hertz-Picciotto, Martin, & Suchindran, 2006). For example, severe maternal depression diminished the protective effects of IQ (Horowitz & Garber, 2003). Further work is clearly needed in this area.

Parents with a Chronic Illness

Parents with chronic diseases or health conditions, such as chronic pain, multiple sclerosis, or even cancer, often face additional challenges in promoting the healthy and adaptive functioning of their young children. Due in part to the long-term nature of these conditions, unpredictability/stress, alterations in family roles and responsibilities, and the limited physical, psychological, and financial resources that are often present, children of parents with chronic diseases and health conditions are typically considered a group at risk for deleterious outcomes (Pakenham & Cox, 2012). However, a surprisingly restricted research base has addressed a range of parental chronic health conditions and the impact of these conditions on children, both concurrently and over time (Anderson, Huth, Garcia, & Swezey, 2014).

Approximately 10% of U.S. children live in households in which a parent has a chronic medical condition and/or illness (Barkmann, Romer, Watson, & Schulte-Markwort, 2007; Sieh, Meijer, Oort, Visser-Meily, & Van der Leij, 2010). Several recent reviews and meta-analyses suggest that children of parents with chronic medical conditions and/or illnesses have been found to exhibit greater mental health difficulties, such as depression and anxiety, as well as behavioral problems, when compared to children of healthy parents (Bogosian, Moss-Morris, & Hadwin, 2010; Diareme et al., 2007; Krattenmacher et al., 2012; Sieh et al., 2010; Umberger, 2014). These findings hold despite the vast age ranges of children and the variety of parental health conditions and illnesses included in these studies.

However, moving beyond the simple presence or absence of a health condition, researchers have recently begun to examine whether comorbidity between mental and physical health conditions may exacerbate the risks on children. For example, Razaz and colleagues (2015) examined the association

between parental multiple sclerosis (MS) and comorbid physical and mental health factors, and young children's development (age 5) in a large population-based study. Their findings indicate that the presence of parental MS alone was actually associated with lower rates of vulnerability in social development. However, children whose mothers had both MS and other comorbid physical and mental health problems were at an increased risk for language, cognitive, and physical development vulnerabilities (Razaz et al., 2015). These findings suggest that comorbidity between physical and mental health problems in caregivers may be particularly detrimental for young children's development.

Other work has focused on the impact of sudden changes in parental health, sometimes referred to as parental health "shocks" (Mühlenweg, Westermaier, & Morefield, 2015) on preschoolers emotional and social development. Taking an economic perspective, Mühlenweg and colleagues (2015) hypothesized that changes to parental health may limit the family's financial resources and decrease the quality of parent–child interactions, both of which negatively impact the "investments" made on the child, particularly when these changes in physical health occur early in child development. In a large German sample of close to 20,000 adults, parental health shocks occurring during infancy and early childhood predicted children's symptoms of emotional problems, hyperactivity, and conduct problems at age 6 (Mühlenweg et al., 2015).

Given that children of parents with both mental and physical illness are at risk for worse outcomes than children of healthy parents, Krattenmacher and colleagues (2014) directly compared the impact of parental cancer with that of parental mental illness on children and adolescents. Children of a parent with mental illness were more likely than children of a parent with cancer to exhibit emotional and behavioral problems; however, after adjusting for socioeconomic status, these results were no longer significant. Interestingly, there appeared to be significantly greater consistency in the ratings of the child's emotional and behavioral problems in families with parental cancer as opposed to families with parental mental illness (Krattenmacher et al., 2014). In families with cancer or mental illness, the healthy parent's health-related quality of life also emerged as an important predictor of child outcomes in both groups, such that mental and physical health-related quality of life predicted children's emotional and behavioral problems. Thus, while there are higher than normal rates of emotional and behavioral problems in children of a parent with cancer and children of a parent with mental illness, both groups appear to have more similarities than differences in terms of negative child outcomes.

Harsh and Inconsistent Discipline

Despite the known long-term, negative effects of harsh discipline of children, it remains a common parenting practice in the United States (Gershoff, 2008; Kim, Pears, Fisher, Connelly, & Landsverk, 2010; Regalado, Sareen, Inkelas, Wissow, & Halfon, 2004; Runyan et al., 2010; Straus & Field, 2003). Two important components appear to be common to harsh parenting: (1) The child experiences pain or discomfort, and (2) the parent's intent is to correct or

punish the child's behavior (Harder + Company Community Research, 2012). The latter has been widely expressed by parents as their reason for engaging in such parenting practices; however, it has clearly been shown that harsh parenting does not improve a child's behavior in the long term (Gershoff, 2013). While "harsh parenting" has been defined in multiple ways, most definitions typically include physical (i.e., spanking) and/or verbal (i.e., scolding, yelling, being coercive) discipline and include a wide range of behaviors with considerable variations in severity. This severity continuum suggests that harsh parenting runs the high risk of escalating to the level of child maltreatment (discussed later in this chapter). This pattern has been noted in datasets on child abuse and neglect, because most documented cases of physical abuse begin with parents physically punishing their children for a perceived misdeed (Gershoff, 2013).

Harsh parenting has its origins in the interplay of parent upbringing, parent psychopathology, attribution of child intentionality, lack of exposure to healthy parenting models and parent–child relationships, authoritarian parenting styles, and family dysfunction (Belsky, Jaffee, Sligo, Woodward, & Silva, 2005; Bert, Guner, & Lanzi, 2009; Burchinal, Skinner, & Reznick, 2010; Frias-Armenta & McCloskey, 1998; Kim et al., 2010). Multiple bodies of research, spanning the globe, have established a clear link between harsh discipline and behavioral problems in young children. For instance, studies using longitudinal and nationally representative data have demonstrated that spanking in early childhood predicts increases in children's problem behavior over time across white, black, Latino, and Asian subsamples (Berlin et al., 2009; Gershoff, 2013; McLoyd & Smith, 2002). Infants and toddlers in Australia were followed from ages 7 months to 36 months, and researchers found that parent stress and harsh discipline were consistent and cumulative predictors of externalizing behaviors (Bayer, Hiscock, Ukoumunne, Price, & Wake, 2008). A study of more than 3,000 preschoolers revealed that increases in spanking during the toddler years predicted increases in preschool-age aggression, over and above effects of initial levels of maternal warmth (Lee, Altschul, & Gershoff, 2013). In another study spanking (but not verbal punishment) at age 1 predicted child aggression at age 2 and lower Bayley mental development scores at age 3 (Berlin et al., 2009), suggesting that the experience of harsh discipline not only impacts behaviors but also influences cognitive development in a negative and concerning manner.

Harsh parenting continues to impact children throughout development. Significantly higher rates of depression and externalizing behaviors in adolescents are associated with both parents' use of harsh discipline (Bender et al., 2007). In examining variables that influence the course of depressive episodes in college students, harsh discipline in childhood was shown to have a significant negative impact on depression severity and relapse (Lara, Klein, & Kasch, 2000). Lasting effects of harsh parenting in childhood have been shown to be present in the realm of relational functioning in adulthood. A longitudinal study of adolescents indicated that harsh physical punishment in childhood is linked with greater perpetration of violence against an intimate partner later in life (Swinford, DeMaris, Cernkovich, & Giordano, 2000).

The findings clearly demonstrate the negative consequences of harsh parenting across developmental stages.

While there is clear evidence that the experience of harsh parenting is detrimental to a child's early development and long-term behavior, the mechanisms are less clear. Transactional and ecological perspectives tell us that harsh parenting and subsequent outcomes are the result of an interaction of subsystems between a child and his or her environment and it is therefore difficult to isolate a single pathway of effect. It is likely that a combination of child and parent factors contributing to harsh parenting and negative outcomes (Gershoff, 2013). For example, during the second year of life, children normatively begin to challenge parental authority, and this has been associated with the onset and increased use of harsh parenting (Kim et al., 2010). It has been suggested that a cycle forms in the early parent–child relationship whereby children's negative emotionality and harsh parenting practices reinforce one another and persist past early childhood (Patterson & Fisher, 2002; Scaramella, Neppl, Ontai, & Conger, 2008). Both infant negative emotionality (Lipscomb et al., 2011) and fussiness (Berlin et al., 2009) have been linked to increases in harsh discipline.

Similar to how a combination of risk factors may give rise to harsh parenting and its negative consequences, there are also protective factors that diminish the likelihood of this pattern, such as early maternal warmth and support. For example, in a study of rural families in Iowa, parents who were treated harshly by their own caregivers tended to emulate these behaviors with their children. However, if they coparented with a partner who demonstrated a warm and supportive parenting style, the intergenerational continuity was more likely to be disrupted (Conger, Schofield, & Neppl, 2012). In a community sample of over 2,500 school-age children, parental warmth served as a buffer to the damaging influences of harsh physical discipline (McKee et al., 2007). Maternal emotional support was also shown to moderate the link between spanking and problem behavior in young children (McLoyd & Smith, 2002). These findings are consistent with emerging research in developmental neuroscience that assert that early maternal support is associated with larger brain structure volumes in children (Luby et al., 2012, 2013). Some aspects of resilience may be systematically learned or internalized through the parent–child relationship (Merrell, Whitcomb, & Parisi, 2009), with parents playing an important role in shaping a child's inherent skills for adaptive coping in adverse conditions.

Inconsistent parenting is characterized by partial, recurrent, and unpredictable breakdowns in parental control (Berg-Nielsen, Vikan, & Dahl, 2002) and the use of disparate practices across time and between parents (Gardner, 1989). It is often grouped with investigations on harsh parenting, largely due to similar quality, origins, and effects. However, inconsistent parenting is qualitatively different, because it does not necessarily focus on the parental tendency to react negatively to the child, and it places more emphasis on ineffective and/or erratic parenting practices. Furthermore, it has been shown that

inconsistent parenting can have a different effect than harsh parenting (or the combination; Surjadi, Lorenz, Conger, & Wickrama, 2013) and should be investigated as a separate construct in future studies.

Overall, there is limited research on the effects of inconsistent parenting in the early years and only a minimal amount focused on older children. It has been suggested that a general continuity exists in childrearing practices from early childhood to early adolescence (Holden & Miller, 1999; Roberts, Block, & Block, 1984). Therefore, it can be hypothesized that, similar to older children, young children are likely to experience this type of discipline and its potential negative effects. This parenting style has been associated with negative child outcomes (Stoneman, Brody, & Burke, 1989) and is considered to be a contributor to conduct problems and anxious behavioral patterns in childhood and adolescence (Cerezo & D'Ocon, 1995; Dodge, Coie, & Lynam, 2006; Dwairy, 2008; Gardner, 1989; Patterson, DeBaryshe, & Ramsey, 1989; Yap, Pilkington, Ryan, & Jorm, 2014). These associations are likely to exist due to the ongoing hypothesis that parents who provide mixed, inconsistent consequences increase the resistance to extinction of the child's problem behavior (Patterson, 1976). Additionally, when a child develops in unpredictable surroundings, there is chronic uncertainty and an inability to predict the reactions of persons in his or her immediate environment. Some children may develop feelings of not being able to influence events in their surroundings, a helplessness that may predispose them to anxiety, or they may become disruptive and use manipulation as a coping mechanism to control their unstable surroundings (Berg-Nielsen et al., 2002).

In addition, there is little evidence on protective mechanisms that offset the impact of inconsistent parenting. For example, positive emotionality in the child may be one way for school-age children to decrease the risk of adjustment problems in response to inconsistent parenting (Lengua, 2002; Masten et al., 1999). Parenting interventions can also have an impact on inconsistent discipline and positive child adjustment. In studying the effectiveness of a group-based parent training for parents and their children (ages 2–12 years), it was shown that the treatment group had positive changes in child externalizing behaviors and improved positive parenting, which included lower levels of inconsistent discipline (Kjøbli, Hukkelberg, & Ogden, 2013). This study utilized parent management training (the Oregon model; Forgatch & DeGarmo, 1999), which targets a number of factors common to separated parents, including interparental conflict and discipline. In summary, there is clearly a need for more research to understanding the specific effects of inconsistent parenting (vs. harsh parenting), the impact during the child's early years, and identification of pathways to resilience.

Early Deprivation

Institutional rearing is characterized by social deprivation, no exposure to sensitive caregiving and contingent responsiveness, and therefore limited

opportunities for children to form selective attachments (Fox, Almas, Degnan, Nelson, & Zeanah, 2011; Zeanah et al., 2003). This type of deprivation has been associated with a variety of maladaptive outcomes in the developmental, brain, and clinical domains (Smyke, Zeanah, Fox, & Nelson, 2009; Vorria, Rutter, Pickles, Wolkind, & Hobsbaum, 1998; Zeanah et al., 2003). Two influential studies assessing the effects of deprivation are the English Romanian Adoptees (ERA) study (Rutter, 1998; Rutter, Sonuga-Barke, & Castle, 2010) and the Bucharest Early Intervention Project (BEIP; Zeanah et al., 2003). The ERA study identified children who were raised in Romanian institutions and later adopted into families living in the United Kingdom. These children were compared to a control group of infants and young children who were born in the United Kingdom and adopted into similar British families. The BEIP was a randomized controlled trial of foster placement as an alternative to institutionalization in abandoned infants and toddlers. The BEIP is unique in that it was able to follow children during the time of institutional rearing and after adoption. Relevant findings from these studies and others are discussed.

Researchers have concluded that early neglect as a result of institutional deprivation has a lasting impact on cognitive functioning. A meta-analysis of more than 75 studies (van IJzendoorn, Luijk, & Juffer, 2008) found a significant effect on IQ, with children growing up in institutions having substantially lower IQ scores. The age of adoption of these children appears to be critical in the trajectory of their intellectual development. Significant effects of adoption age were also found in the ERA study. At the time of adoption, infants and young children arriving from Romania had significant delays in their intellectual development (Rutter, 1998). By the time these children were 4–6 years of age, those who were below the age of 6 months when adopted appeared to catch up to their U.K.-born adopted controls. However, there was a significant negative correlation between age of adoption and IQ for children adopted from Romania after 6 months of age (Castle et al., 1999).

Similar results were uncovered in the BEIP longitudinal study (Fox et al., 2011). Intellectual and developmental measures obtained at three time points (30, 42, and 54 months of age) indicated significantly better development in the foster care group than in those with continued institutional rearing, though it remained significantly worse than that in the community sample of children. When examining the ability of children to recover, it was shown that the younger the child when placed in foster care, the more the cognitive gains, with little improvement for children older than 24 months of age at the time of placement. Furthermore, gains in IQ were particularly evident for those children who remained with their intervention family, highlighting the importance of consistency. The course of language development also demonstrated similar patterns. Both expressive and receptive language were significantly better in the foster care group compared to those with continued institutional rearing; however, the foster care group did not attain the language level of the community sample group. These data suggest the continued importance of

early nurturance and stimulation, and the negative effects of severe psychosocial deprivation on the development of IQ scores across early childhood.

The impact of early deprivation on brain development and functioning is another important area of inquiry of the BEIP. Brain functioning was assessed by EEGs and event-related potentials (ERPs). The findings indicate more general brain activity and hemispheric differentiation for children who had been placed in foster care at younger ages (Smyke et al., 2009). Specifically, foster care was shown to be partially effective in ameliorating deficits caused by institutionalization. At three time points, institutionalized children showed markedly less brain activity and longer processing speed times compared with noninstitutionalized children. By age 42 months, the levels of institutionalized children who were then placed in foster care fell between the brain function levels of the institutionalized and noninstitutionalized children, showing some recovery in the context of a secure and stable caregiving environment. Another study by BEIP researchers (McLaughlin et al., 2010) revealed a reduction in a specific pattern of brain activity that signified a delay in cortical maturation for institutionalized children. This pattern significantly predicted symptoms of hyperactivity and impulsivity at 54 months of age. Other research has shown that early deprivation has negative impacts on metabolic rates of specific brain regions (Chugani et al., 2001), structure of brain regions that have implications for limbic system functionality (Eluvathingal et al., 2006), and amygdala volumes (Mehta et al., 2009).

In the realm of clinical disorders, children reared in institutions evidence greater symptoms of attention-deficit/hyperactivity disorder (ADHD), anxiety, depression, disruptive behavior disorders, and attachment disturbances (Chugani et al., 2001; Eluvathingal et al., 2006; Mehta et al., 2009; Walker et al., 2011). Several major areas of clinical functioning were assessed as part of the BEIP. It was found that there was no demonstrated benefit of foster care for reducing externalizing disorders at 54 months of age among the institutionalized children (Smyke et al., 2009). However, there was a significant reduction in internalizing disorders at 54 months for children in foster care compared to children who remained in the institutions. Humphreys et al. (2015) examined psychopathology at age 12 as part of the BEIP study using a community sample as a comparison group. It was found that the children who had been placed in an institution had higher symptom counts for internalizing disorders, externalizing disorders, and ADHD than did children who had never been placed in an institution. In addressing early intervention, compared with the children who remained under institutionalized care, the children in foster care had fewer externalizing symptoms. In further analyses, symptom scores differed by stability of foster care placement.

Strong intervention effects for attachment were found in the BEIP study. Significantly more children in foster care had secure attachments at 42 months of age than did children who remained in institutions. However, the children in foster care did not demonstrate secure attachment at the levels of children who had never been institutionalized. Evidence of attachment disorder

behaviors was also obtained as part of the ERA study (O'Connor, Bredenkamp, & Rutter, 1999). Results indicated that attachment disorder behaviors were positively associated with duration of severe deprivation, but a substantial number of children exposed to even prolonged, severe early deprivation did not exhibit these symptoms, suggesting pathways of resilience for some children exposed to severe deprivation.

It can be concluded that deprivation early in life has devastating effects. Although the effects are quite profound, there are opportunities for recovery for these children. Placement into therapeutic foster care provides a protective effect, with research indicating that timing and stability of foster care are crucial for positive adaptation. The finding that therapeutic foster care can produce a partial recovery for these children, especially for IQ and brain functioning, also suggests a possible sensitive period in cognitive and brain development.

Child Maltreatment

Child maltreatment encompasses acts of commission or omission by a caregiver that result in harm, potential for harm, or threat of harm to a child, even if harm is not intended (Gilbert et al., 2009; Leeb, Paulozzi, Melanson, Simon, & Arias, 2008). Widely recognized forms of maltreatment are physical abuse, sexual abuse, emotional abuse, and neglect. Every year, about 4–16% of children are physically abused, and 1 in 10 is neglected or psychologically abused (Kaplow & Widom, 2007). Determinants of maltreatment are similar to harsh parenting (see earlier discussion). Income, parental education, and socioeconomic inequalities are known to be significant risk factors (Gilbert et al., 2009).

Maltreatment in early childhood is associated with serious physical risk, as well as specific insults to cognitive, social, and emotional development (Putnam-Hornstein, 2011; Zeanah et al., 2001). Early maltreatment has been shown to be particularly deleterious with respect to enduring negative patterns of emotion regulation, social relatedness, and executive functioning (Bolger, Patterson, & Kupersmidt, 1998; Cowell, Cicchetti, Rogosch, & Toth, 2015; Zeanah, Fox, & Nelson, 2013). Related to salient developmental issues in early childhood, maltreatment is associated with insecure and disorganized/disoriented attachments to caregivers (Cicchetti & Barnett, 1991) and less developed language expression for internal states and feelings about the self and others (Beeghly & Cicchetti, 1994). Numerous studies indicate that child maltreatment increases the risk for developing internalizing (i.e., anxiety, depression) and externalizing (i.e., aggression, acting out) disorders (English et al., 2005; Fergusson, Boden, & Horwood, 2008; Herrenkohl & Herrenkohl, 2007; Lansford et al., 2002; Manly, Kim, Rogosch, & Cicchetti, 2001). These symptoms persist through adolescence, as indicated by the finding that childhood maltreatment is significantly associated with both internalizing and externalizing behaviors at age 14 (Mills et al., 2013). There are also identified associations with antisocial behaviors. Children who were maltreated in early childhood

(ages 0–54 months) were found to be at greater risk for developing antisocial behaviors in adolescence (Egeland, Yates, Appleyard, & Van Dulmen, 2002).

Characteristics of child maltreatment can alter the course and severity of negative impact. Children who are exposed to one type of maltreatment are often exposed to other types on several occasions or continuously. Repeated episodes of maltreatment and experiences across subtypes are associated with increased risk of severe maltreatment and predict worse outcomes across a number of domains (Jonson-Reid, Kohl, & Drake, 2012; Lau, Leeb, English, Graham, Briggs, et al., 2005). Behavioral outcomes are also determined by the early timing of maltreatment. Researchers have found that children with exposure to maltreatment in infancy have significantly greater difficulties with self-control and regulation than children maltreated later in childhood (Cowell et al., 2015). Based on these findings, the authors assert that young children are particularly vulnerable to the effects of maltreatment due to the rapid development of neuronal connections and major brain organization that occurs at this time.

Protective factors that offset the effects of maltreatment are present within various environmental subsystems. In the realm of caregiving and family relationships, stable foster care, the presence of a caring and supportive adult, and positive family changes have all been related to resilience (Cicchetti & Rogosch, 2009; Egeland, Carlson, & Sroufe, 1993; MacMillan, 2011; Romans, Martin, Anderson, Herbison, & Mullen, 1995; Spaccarelli & Kim, 1995; Toth & Cicchetti, 1996; Valentine & Feinauer, 1993). Within school and community settings, a structured school environment, social support, involvement with a religious community, and involvement in extracurricular activities or hobbies have all been related to positive adaptation (Cicchetti, 2013; Egeland et al., 1993; Herrenkohl, Egolf, & Herrenkohl, 1997; Jaffee, Caspi, Moffitt, Polo-Tomas, & Taylor, 2007; Valentine & Feinauer, 1993).

In summary, child maltreatment represents an alarmingly prevalent and highly detrimental influence on the development of young children. The long-lasting consequences of child maltreatment on children and society are substantial and warrant increased investment in preventive and therapeutic strategies in early childhood that address not only the child but also the caregiving systems in which they operate. There is promising evidence that interventions have been effective in reducing risk and recidivism rates of abuse and neglect in early childhood at the level of parent training (Letarte, Normandeau, & Allard, 2010; Webster-Stratton & Reid, 2010) and in collaboration with the child welfare system (Constantino, Ben-David, Navsaria, Spiegel, Glowinski, et al., 2016; Zeanah et al., 2001).

FAMILY FACTORS

Family characteristics have changed drastically in the recent decades, and preschoolers in the 21st century often grow up with two working parents;

experience divorce; and live with single parents, blended families, and same-sex couples. Family factors can impart both risk and resilience on preschool social–emotional development, and there are no uniform outcomes or consequences that ensue following exposure, because individual characteristics and transactional processes also play influential roles. However, we repeatedly see that the preschool years appear to be an especially sensitive period in which the effects of family factors are more pronounced.

Marital Discord

Some level of marital discord and arguments are present in all two-parent families. Yet high levels of marital discord and interparental conflict are associated with increased psychological adjustment problems, including both internalizing and externalizing disorders, in all ages of children (Emery, 1982; Grych & Fincham, 1990). Moreover, these effects appear to be especially pronounced in the preschool period (Kitzmann, Gaylord, Holt, & Kenny, 2003). Preschool appears to be a sensitive period for parental conflict, because preschoolers exhibit increased fear and threat reactivity, and a lack of developed coping efficacy in response to the conflict (Cummings, Vogel, Cummings, & El-Sheikh, 1989; Grych, 1998; Jouriles, Spiller, Stephens, McDonald, & Swank, 2000). Preschoolers also appear to be more vulnerable to the effects of marital discord given that children's cognitive and social perspective-taking abilities develop during the preschool years (Davies, Sturge-Apple, Winter, Cummings, & Farrell, 2006). These abilities enable the child to experience more concern about the parents' welfare during conflicts, which leads to more attempts to diffuse the situation (Davies et al., 2006). In fact, preschoolers' emotional reactivity to conflict predicted increased internalizing symptoms, while children's involvement in interparental conflict predicted increased externalizing problems 1 year later (Davies, Coe, Martin, Sturge-Apple, & Cummings, 2015). Preschoolers who were more emotionally reactive *and* also exhibited increased involvement in interparental conflict prospectively demonstrated the highest internalizing and externalizing disorders 1 year later (Davies et al., 2015).

It has been hypothesized that when children are exposed to marital discord, the underlying mechanism associated with more maladaptive emotional adjustment is emotional insecurity (Cummings & Davies, 1996). Compared to a sense of "emotional security," which is defined as a sense of security, safety, and protection that leads to optimal social–emotional regulation, "emotional insecurity" is associated with heightened emotional reactivity and behavioral dysregulation, avoidance, or overinvolvement in conflict (Cummings & Davies, 1996). Kindergartners exposure to marital conflict has been shown to increase emotional insecurity in second grade, which subsequently predicts increased adolescent internalizing and externalizing symptoms in seventh grade (Cummings, George, McCoy, & Davies, 2012). Exposure to marital conflict during the preschool period is associated with especially elevated risk

that may promote cascade effects and transactional processes as emotional insecurity in the family develops over repeated instances of marital discord, which influences problems such as externalizing symptoms, as well as more general interpersonal dysfunction, such as social competency (Kouros, Cummings, & Davies, 2010).

Although marital conflict can increase risk for difficulties later in childhood and young adulthood, not all conflict is alike. Some marital conflict can be adaptive and lead to resilience in youth. For instance, constructive conflict (problem solving, affection, and support between parents during conflict) has been shown to reduce child aggressive tendencies (Cummings, Goeke-Morey, & Papp, 2004) and may facilitate the child's own problem-solving and coping abilities (Grych & Fincham, 1999). Destructive conflict, on the other hand, characterized by hostile, angry, threatening tactics and use of aggression and personal insults, is associated with the maladaptive outcomes mentioned earlier (Cummings & Davies, 1994; Grych & Fincham, 1993). Additionally, constructive and destructive marital conflict appear prospectively to increase or decrease children's emotional security, respectively, which also leads to increases or decreases in children's prosocial and adaptive behaviors (McCoy, Cummings, & Davies, 2009). It should be noted that the distinction between constructive and destructive conflict has mostly been examined in older children; therefore, it is still unknown how constructive conflict may promote resilience in preschoolers. Given that conflict appears to have stronger ramifications for preschoolers compared with older children (Kitzmann et al., 2003), constructive marital conflict may help to provide even stronger scaffolding of adaptive self-regulatory and interpersonal functioning that promote adaptive developmental cascades.

Divorce

After ongoing marital discord and conflict with no resolution, divorce may follow. In some instances, divorce can be beneficial for a preschooler, because it removes the child from a high-conflict environment and results in fewer cumulative stressors and fewer risk factors associated with maladaptive psychological adjustment (Amato, Kane, & James, 2011). In fact, preschooler's antisocial behaviors decrease when high-conflict marriages dissolve (Amato, Loomis, & Booth, 1995; Strohschein, 2005), and children whose parents had a poor marital relationships and stayed together had more behavior problems and lower prosocial behavior compared to children whose parents had poor marital relationships and subsequently divorced (Heinicke, Guthrie, & Ruth, 1997). Divorce has also been shown to have some small positive effects on preschoolers' interpersonal functioning (Kunz, 2001).

However, the concept of a "good divorce" has not been well-supported (Amato et al., 2011), and a much larger body of literature indicates that divorce commonly results in increased risk for behavioral, psychological adjustment, and academic functioning problems in children (Amato, 2001, 2010). In fact,

an earlier age of divorce (i.e., the preschool years) is associated with higher risk of internalizing and externalizing disorders later in childhood, compared with divorce during childhood and adolescence (Lansford et al., 2006). In fact, divorce prior to age 6 (rather than after age 6) is associated with more anxiety and depression, more hyperactive, disobedient and defiant behavior, lower attachment to parents during adolescence, and perceiving parents as less caring (Pagani, Boulerice, Tremblay, & Vitaro, 1997; Strohschein, 2005; Woodward, Fergusson, & Belsky, 2000).

Theory purports that children under the age of 6 lack the cognitive development and ability to understand the concept of divorce, leading to high levels of confusion, fear of abandonment, neediness, and acting-out behaviors in preschoolers (Emery, 1999). Additionally, preschool-age children often blame themselves for their parents' divorce due to cognitive egocentricity (Leon, 2004; Rogers, 2004). Others have posited that cumulative stress is to blame for the more harmful effects of divorce evidenced during the preschool years. The earlier in the child's life the divorce occurs, the more cumulative stressors and risk factors the child will be exposed to (Kalter & Rembar, 1981). Divorce, in and of itself, is a stressor; however, divorce is also often subsequently associated with many other risk factors, such as financial strain, less stable environments with more familial transitions, parental experience of psychopathology, and separation anxiety and attachment difficulties with parental figures (Fomby & Cherlin, 2007; Lansford, 2009; Rogers, 2004). Again, it appears that contextual and individual differences moderate the effects of divorce to impart elevated risk or resilience for preschoolers.

Absence of Fathers

One of the most obvious risk factors associated with divorce is decreased involvement of the non-resident parent, often the father. Whether due to divorce, family changes, or single parenthood, the absence of fathers has repeatedly been shown to lead to negative outcomes throughout childhood, including internalizing and externalizing disorders (Amato, 2010). Especially for boys, fathers provide economic resources, discipline, a role model, and guidance (Silverstein & Auerbach, 1999), and during the preschool years, fathers are demonstrated to be key figures in attachment (George, Cummings, & Davies, 2010) and are associated with a decrease in problem behaviors (Aldous & Mulligan, 2002) and an increase in social skills (Katoh, Ishii-Kuntz, Makino, & Tsuchiya, 2002). Father absence at age 3 predicts an increased probability of the child having more emotional, conduct, and peer problems at age 5, and father absence at age 5 predicts these same difficulties at age 7, demonstrating that father absence in preschool plays a causal and cascading role in the onset of problem behaviors during childhood (Flouri, Midouhas, & Narayanan, 2015). At the same time, this study also found that severe conduct and peer problems and child hyperactivity at age 3 also predicted a higher probability that the father would be absent at age 5, indicating

some transactional processes between preschool externalizing behaviors and future father absence (Flouri et al., 2015).

It should be noted that in the Flouri et al. (2015) study, "father absence" was defined as a father not living at home in a coupled relationship. Of course, in many cases of divorce or separation, the father may not live at home but still maintain a relationship with the children. The extent to which the nonresident parent is involved in authoritative parenting by providing emotional support, helping children problem-solve, and helping with homework has been associated with increased resilience as a result of greater child well-being and adolescent functioning (Amato & Gilbreth, 1999; Carlson, 2006). Similarly, when biological fathers are absent, stepfathers can provide scaffolding for future mental health. However, some research indicates that blended families may be associated with poorer mental health in preschool-age children (Pearce, Lewis, & Law, 2013), and preschoolers whose mothers cohabitate with a male other than the children's father exhibit poorer literacy skills compared to children whose mothers did not cohabitate (Fagan, 2013). The literature examining mental health outcomes of preschool children in blended U.S. families is sparse, and future research would benefit from examining the effects of these transitions and differing life situations on preschool social–emotional outcomes.

COMMUNITY FACTORS

Various community factors are associated with risk and resilience in preschool children, including family poverty, housing conditions, neighborhoods, and day care/schooling. These can be considered contexts that may shape development, physical/mental health, and school readiness, among other outcomes.

Socioeconomic Status

A robust literature exists examining the impact of poverty on child outcomes and generally concludes that low socioeconomic status (SES), poverty, and greater psychosocial adversity lead to problematic outcomes in youth, particularly during early childhood (McLoyd, 1998). Recent estimates indicate that 17.4% of children living in poverty have early-onset behavioral problems (Holtz, Fox, & Meurer, 2015), and that income alone explains up to 6% of the variance in preschool outcomes (Kohen & Guèvremont, 2014). Moving beyond simple associations, research has increasingly attempted to focus on mediating and moderating mechanisms that may explain the links between poverty and child outcomes. For example, one recent study examined salivary interleukin (IL)-1β levels in preschool children who had experienced traumatic stress (e.g., maltreatment) and contextual (e.g., low family income) stressors (Tyrka, Parade, Valentine, Eslinger, & Seifer, 2015). Current and lifetime contextual stress, as well as traumatic stress, had significant effects on IL-1β

levels. These findings are significant, because IL-1β is hypothesized to be associated with the neuropathology of psychiatric disorders.

Other work suggests that poverty negatively impacts the developing brain (Hair, Hanson, Wolfe, & Pollak, 2015; Luby, 2015). Hair and colleagues (2015) found that children (ages 4–22) living below federal poverty limits had smaller volumes in several important brain regions including gray matter, frontal and temporal lobes, and the hippocampus. Furthermore, the decreased volume in the frontal and temporal lobes explained approximately 15–20% of the variance in academic achievement in the sample. In addition, maternal support experienced during the preschool period has been shown to mediate the negative effects of poverty on brain development (Luby et al., 2013).

These findings have critical public health implications, since aspects of the child's environment influence many, if not all, facets of preschool development, including psychosocial and physiological indices. Growing up with prolonged disadvantage and adversity lead to cognitive and noncognitive skills deficits later in life (Heckman, 2006). Furthermore, it is difficult to separate the effects of poverty and lower income from the effects of other commonly co-occurring risk factors, such as low-quality child care, unsafe neighborhoods, single-parent families, and nutritional inadequacy. Thus, children growing up in financially disadvantaged households often experience additional disadvantages across multiple systems and conditions.

Neighborhoods

As stated earlier, neighborhoods can exert a strong influence on the development and outcomes of young children, particularly when combined with other risk factors, such as poverty. It is no surprise that living in economically and socially disadvantaged neighborhoods is associated with negative behavioral and emotional outcomes in children (Leventhal & Brooks-Gunn, 2000). Neighborhood may influence development and outcomes in young children for several reasons. First, exposure to violence and traumatic events is more likely in lower-income neighborhoods, which may lead to increased risk for emotional and behavioral problems. Parental resources, both financial and emotional, are often limited in low-income, impoverished neighborhoods, decreasing a child's opportunities to learn. In many low-income neighborhoods, there are fewer opportunities for physical activity and safe play, which may influence children's physical and mental health. Finally, some low-income neighborhoods offer few (if any) locations to purchase healthy food and receive quality health care, which may also impact young children's development over time. In a recent review of 32 studies focusing on physical aspects of young children's neighborhoods, the authors conclude that neighborhoods with more green spaces and less traffic facilitate more optimal child health and development (Christian et al., 2015). Furthermore, the presence of more child-relevant destinations, such as libraries and schools, was positively associated with enhanced physical and mental health for young children.

Emerging research has also linked neighborhood quality to specific

outcomes during early childhood, such as obesity. In a large sample of preschoolers (over 11,000), higher rates of homicide in the neighborhood was associated with a 22% higher prevalence of obesity among children living in that neighborhood (Lovasi et al., 2013). This study also found that more green space, as measured by tree density, was associated with a decreased prevalence of obesity among preschoolers. Other work indicates that obesity in preschoolers is also predicted by the availability of fast-food restaurants in the area, particularly in lower-income and urban areas (Newman, Howlett, & Burton, 2014).

Day Care

Quality of child care appears to be an important contributor to later child outcomes. Given that most U.S. children are enrolled in child care for at least a portion of their lives, the issue of developmental outcomes and child care duration, timing, and quality has received increasing interest. One of the first investigations of maternal employments and child care used data from the Children of the National Longitudinal Survey of Youth (NLSY; Baydar & Brooks-Gunn, 1991). The findings indicate that maternal employment during the child's first year of life has significant negative effects on cognitive and behavioral outcomes during preschool, but that maternal employment during the second or third year of life does not. Furthermore, nonparental child care arrangements influence behavioral problems for all children and cognitive development for children in poverty. Not surprisingly, this research (and that of others) has created a large debate on the developmental costs and benefits of child care, particularly for young children.

Using a more recently recruited group of children from the Millennium Cohort Study (Côté, Doyle, Petitclerc, & Timmins, 2013), attendance in child care during the first year of life was associated with enhanced cognitive outcomes during preschool, but only among children whose mothers had lower levels of education. However, the cognitive changes in the group did not persist beyond age 3. In a different longitudinal cohort study of 1,269 families, participating in child care during early life reduced academic inequalities up to early adolescence for children with lower SES (Laurin et al., 2015). The results from this study suggest that both high-intensity (greater than 35 hours per week) and early-onset (5 months of age) child care experiences led to academic benefits persisting until age 12, but only for children with lower SES.

Other research has drawn seemingly opposing conclusions. In a nationally representative sample of more than 6,000 children (Coley, Votruba-Drzal, Miller, & Koury, 2013), early use of child care (e.g., beginning at age 9 months and younger) and/or for extended hours each day (e.g., 25 hours or more per week) was associated with negative child outcomes, such as learning problems in kindergarten and externalizing behavior problems in preschool and kindergarten. Using data from the Early Childhood Longitudinal Study—Kindergarten Cohort (ECLS-K), Loeb, Bridges, Bassok, Fuller, and Rumberger (2007) found that enrollment in a center-based child care

program prior to kindergarten was associated with a 0.1 *SD* increase in average reading and math skills, but that it is also associated with a similar-size negative effect on self-control, learning, and interpersonal skills. The authors also state that the age of enrollment appears to be predictive, with children beginning child care prior to age 2 exhibiting somewhat lower cognitive skills and significantly more behavioral problems in kindergarten. Furthermore, children from higher income homes enrolled in child care for a greater number of hours per week exhibited substantially greater behavioral problems.

More research needs to focus on the duration of quality care, and it appears that very little is known about the impact of child care on middle- and/or higher-income children. Unfortunately, most high-quality care is expensive, and, as a result, may be less viable for children of families living in poverty who may already be at-risk for a host of negative outcomes.

SPECIAL CONSIDERATIONS

Culture

Cultural differences in parenting behaviors with young children have been reported (Keller et al., 2004; Slade & Wissow, 2004). These include beliefs on how to control a child's behavior, the duty of children, and respect to elders (Lau, 2006), and children's intentionality (Burchinal et al., 2010). For example, preparing a child for potential racial discrimination and danger impacted the sense of urgency for a child to obey in African American families and other families living in unsafe neighborhoods (Dodge, McLoyd, & Lansford, 2005; Ispa & Halgunseth, 2004). This urgency could lead to increased use of harsh disciplinary techniques. An awareness of these underlying cognitions that contribute to the emergence of harsh parenting can create more effective interventions and meaningful interpretations of data for the African American community and others facing similar adversities. Additionally, several studies have shown an absence of negative effects of spanking in African American children (Dodge et al., 2005), which may be explained by the role that spanking plays in teaching survival skills to these children.

Another example of a culturally mitigated parenting belief is in the context of play. There are cultural differences in the frequency and content of play, as well as caregiver–child interactions (Jent, Niec, & Baker, 2011). Some families may value academic components of play (Farver & Shin, 1997), while others may emphasize individualism and self-reliance, preferring more child-directed play. Early choice making in play may be discouraged due to a value emphasis on child obedience and respect (Johnston & Wong, 2002). These dynamics could lead to inaccurate conclusions about play that seemingly deviate from the norm and give rise to interpretations that the parent places less importance on playtime. Although culture is important, it is a difficult construct to operationalize. The measurement of cultural influences in research is difficult, because it is not limited to only the race and ethnicity of an individual. There is a confounding influence of factors associated with culture,

such as acculturation, immigrant status, economic status, income, education and occupation (Harder + Company Community Research, 2012). Therefore, observed differences among different cultural groups should be interpreted with caution due to the confounding nature of the factors related to culture. This can lead one to believe there are cultural differences when there may not be any.

In conclusion, the specific influence of culture on early child development is still unclear in the research literature. However, an understanding of cultural contexts and underlying processes that shape parent behaviors and expectations of childhood can be helpful in the realm of clinical interventions. A global review of research on various types of parenting interventions concluded that the interventions were more effective when adaptations were developed within the context of the parents' culture (Navsaria & Hong, 2016). Quantitative and qualitative investigations of this ecological system are needed to better understand this important, yet minimally researched, construct.

Same-Sex Couples

The American family can take many different forms and in 2014, between 10 and 24% of same-sex couples have children in their homes (including biological and adoptive children) (U.S. Census Bureau, 2014). Overall, research supports the notion that children growing up with same-sex parents demonstrate no significant disadvantages and fare just as well as children growing up with heterosexual parents (Amato, 2012; Moore & Stambolis-Ruhstorfer, 2013; Perrin et al., 2013). However, some research indicates that children and adolescents with lesbian or gay parents experience more depression and marijuana use and lower educational status compared with intact heterosexual families (Regnerus, 2012). It should be noted that these findings are highly controversial and the Regnerus (2012) article has been criticized as using suspect methodology, measurements, and analyses to reach these conclusions (Gates et al., 2012). In fact, subsequent research demonstrates that when these same children are compared with children from divorced or blended families, children of lesbian or gay parents demonstrate minimal differences in these mental health outcomes (Amato, 2012).

Some have speculated that the disparities of outcomes in same-sex couples are due to family transitions and instability rather than the sexual orientation of the parent (e.g., Amato, 2012; Moore & Stambolis-Ruhstorfer, 2013). Initial evidence supports this hypothesis; academic outcomes of children from same-sex parents and heterosexual parents were similar from kindergarten through eighth grade, while the number of family transitions was associated with decreased academic outcomes (Potter, 2012). Given that many adult same-sex couples today started in heterosexual relationships due to stigma and laws against gay and lesbian marriage, many children in same-sex couples have already experienced parental divorce and family transitions. The next generation of research examining same-sex parenting will benefit

from examining children in families in which same-sex parents rear children together, in an increasingly accepting and less-stigmatizing society. Longitudinal studies of same-sex parents compared with the many other types of family compositions in today's society may elucidate risk and protective factors for preschoolers growing up in a variety of family situations.

Technology

There is a growing interest in describing and defining the ways in which technology shapes young children's development and outcomes. In particular, one area that appears to be interesting to investigate is changes in the parent–child relationship or quality of parent–child interactions resulting from Internet-enabled and other electronic devices, such as video games and television.

Research offers support for the negative impact of television and video games on young children's development and outcomes, such as increased rates of obesity (Dennison, Erb, & Jenkins, 2002), attention problems (Christakis, Zimmerman, DiGiuseppe, & McCarty, 2004), and declines in language and cognitive performance (Anderson & Pempek, 2005). In fact, the American Academy of Pediatrics (2001) suggests restricting all television viewing in children younger than age 2 and limiting media exposure to under 2 hours per day in older children. Despite this recommendation, by 3 months of age, close to 40% of children are regularly watching television, DVDs, and videos, and this rates rises to 90% by 25 months of age (Zimmerman, Christakis, & Meltzoff, 2007). In an intervention study, children ages 2 years, 6 months, to 5 years, 5 months, spent approximately 14.5–15.9 hours per week watching TV and playing video games prior to the intervention (Dennison, Russo, Burdick, & Jenkins, 2004). Following the intervention, which took place in child care centers, parents reported a decline of close to 5 hours each week in their child's media exposure, which is significant given that media habits tend to develop and increase during this age.

The exposure to and use of Internet-enabled devices by children has received increased attention in the past decade. Children born within the past 10 years are part of the first generation of youth to grow up with various forms of digital, Internet-enabled technology (e.g., computers, tablets, cell phones, and the Internet) present in their lives from birth. It is estimated that 3.2 billion people worldwide are "online" (International Telecommunications Union, 2015). In fact, a recent study revealed that children ages 12 months to 3 years have access to and use such touch-screen devices for an average of 15 minutes each day (Ahearne, Dilworth, Rollings, Livingstone, & Murray, 2016). Almost one-third of toddlers can perform multiple actions on touch-screen devices, such as swiping and actively looking for features, as well as identify and use specific features (Ahearne et al., 2016). Yet very little is known about the influences that these types of technology may have on promoting risk and resilience during the preschool period, particularly concerning the impact on parent–child relationships and parenting practices. Several recent empirical studies have started to explore the phenomenon of

parenting in the context of Internet-enabled devices such as tablets and cell phones.

Close to 75% of parents who were observed with their children (under age 10) eating in a restaurant used their cellphones during mealtime and 16 of these 55 parents used a cell phone continuously throughout the entire meal with their children. The researchers observed that among parents who were using their cell phones during the meal, the child's bid for attention from the parent (and away from the cell phone) was most often met with a negative parent response, such as facial expressions and scolding (Radesky et al., 2014). To follow up on this intriguing finding, Radesky and colleagues (2015) videotaped over 200 mothers and their 6-year-old children during a structured interaction task that was originally designed to characterize how dyads interact when asked to try different foods. Dyads were then dichotomized based on whether the mother spontaneously used a mobile device during the structured task. 23% of mothers used a mobile device during the discussion task. Interestingly, mothers who used a device initiated fewer verbal and nonverbal interactions with their young children. This pattern of findings has also been replicated in mothers of infants, in that a significant percentage of mothers spontaneously used mobile devices during bottle feeding, and this type of distraction was associated with lower sensitivity to the infant's cues (Golen & Ventura, 2015).

More research is clearly needed to understand fully how mobile device use impacts the parent–child relationship and parent–child engagement, yet the implications from these studies are concerning. Taken together, these results suggest that parents are frequently using mobile devices during typical settings and/or routines when with their young children, and that device use may be linked to reduced parent–child communication. Over time, this may have deleterious consequences, particularly for young children who are more dependent on parents for structuring interactions and promoting continued interactional engagement. While mobile devices and increased access to technology offer many opportunities for growth, learning, and enhanced development, they may also represent a serious, growing risk for the developing preschooler given that devices may stifle and meaningfully alter parent–child interactions and decrease responsiveness to the child. Specifically, the encouragement and exaggerated use of such devices by caregivers appears to be part of a caregiving style characterized by disengagement. For example, when compared to books and other types of toys, electronic toy use among parent–infant dyads resulted in a decreased quality and quantity of parental language, such as words, conversational turns, and responses (Sosa, 2016). This assertion remains to be explored in future research.

CONCLUSIONS

The information provided in this chapter indicates that young children are quite prone to risk, and that further understanding of the factors of

vulnerability and resilience may, in fact, be uniquely important in early childhood. In summary, exposure to biological and psychosocial risks affects the developing brain and compromises the development of children. With cumulative exposure to risks in various contexts, disparities widen and negative trajectories become more firmly established. The presentation of environmental risk at various ecological levels sheds light on the connections among multiple environmental systems for a child that may otherwise appear unrelated or disconnected.

There are a number of critical principles highlighted in this chapter. First, it appears that overall, a sensitive, consistent, and safe caregiving environment is a critical protective factor for this population, especially in the early years. Second, the earlier the risk exposure, the worse the outcome. Conversely, the earlier the intervention, the better the recovery. This clearly suggests a sensitive period to the effects of risk and interventions should be targeted for this time period or earlier as part of preventive endeavors. Third, healthy functioning of a parent is crucial to a child's early experience. Finally, there is strong evidence that underlying neurobiological processes are compromised by, and resilient to, dramatic changes in early experience.

Preventive or other interventions targeting young children and their caregivers are necessary. There is substantial evidence that parenting interventions can improve parent–child relationships, reduce child problem behaviors, decrease the rate of harsh parenting, and prevent maltreatment (Barlow, Johnston, Kendrick, Polnay, & Stewart-Brown, 2006; Gardner, Montgomery, & Knerr, 2015; Piquero, Farrington, Welsh, Tremblay, & Jennings, 2009; Rodriguez, Dumont, Mitchell-Herzfeld, Walden, & Greene, 2010; Selph, Bougatsos, Blazina, & Nelson, 2013). Parents with acute mental illness may be less likely to benefit from parent training; thus, interventions focused jointly on parental psychopathology and parenting may be indicated (Breaux et al., 2014). There has been recent support in the literature on how this two-generation approach to can be more efficacious in reducing risk (Constantino et al., 2016; Shonkoff & Fisher, 2013). Furthermore, appropriate intervention during the early years can also potentially offset negative social and economic outcomes for children and families. For example, early childhood intervention programs in the United States have been shown to have benefits for reducing crime (Aos & Drake, 2013), raising earnings and promoting education (Heckman, 2011), as well as improving adult health (Campbell et al., 2014).

There are limitations to the existing knowledge regarding the effects of early environment and caregiving on children. Most research is focused on adverse outcomes, excluding a deeper understanding of resilience. Future research endeavors should include investigations on understanding resilience over time. Given the transactional nature of the developmental mechanisms, research should focus on how combinations or risk factors work together to increase risk of adverse child development (Goodman et al., 2011). More research is needed on fathers, diverse family structures, and minority and low-income populations. Future work should also utilize advances in neuroimaging

and other techniques to explore the importance of parental support for young children on brain development and other outcomes.

The information presented in this chapter can aid clinicians in early detection and a more precise understanding of environmental factors that may diminish or ameliorate young children's functioning. Ultimately, the extent to which each of these risk factors is causally related to adverse outcomes is hard to establish, because many environmental factors are inextricably clustered. However, while specific effects are unclear, it must be strongly emphasized that decades of research indicate that a combination of environmental risk factors in the early years unequivocally contributes to deleterious outcomes for children. This points to the urgent need for collaborative action among not only clinicians and researchers but also social service agencies, criminal justice systems, insurance companies, and public policymakers to take a comprehensive approach to preventing and reducing impacts of childhood adversity. If not addressed, there will be a lifetime of consequences for child and adult functioning, and ultimately the care of the next generation.

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3

Brain Development during the Preschool Period

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For more than a century, scientists have studied the neural underpinnings of behavior. In the past few decades, developmental neuroscientists have made remarkable advances in understanding the genetic and cellular mechanisms governing the formation of neural circuitry that is important for human cognition. We have been able to understand how neurons form, how their identities are decided, how they connect to form functional groups, and how these connections are modified by experience. In the course of these discoveries, it has become clear that humans have a unique and prolonged period of neurodevelopment that is largely marked by fine-tuning of circuitry beginning postnatally and extending into early childhood, when the foundations of motor, language, and executive functions are established.

In this chapter we discuss the critical period of brain development that occurs postnatally and into the preschool period, with a special emphasis on the brain's most rapid period of dynamic growth in the first 2 years of life. We begin with the mechanisms of brain development and the use of magnetic resonance imaging as a tool for studying the human brain. Following this introduction, we provide a detailed picture of how the brain develops in early life. Afterward we explore genetic and environmental impacts on brain development, sex differences in brain morphology, the role of brain development in cognitive development, and review studies of brain development in those at risk for neurodevelopmental disorders.

MECHANISMS OF PRENATAL AND POSTNATAL BRAIN DEVELOPMENT

Prenatal Development

Brain development is governed by both genetic mechanisms and environmental exposures. Timed, spatially defined gene expression determines how the brain wires itself by controlling the birth, differentiation, and migration of neurons and their synaptic connectivity. After their birth, neurons take on a distinct morphology, migrate to a specific location, and make connections with a target cell population. These processes take the brain, which begins with a smooth (lissencephalic) surface, and shape it into a convoluted structure wired together by axonal fiber bundles.

Neurogenesis and Migration

Brain development begins around the second week of gestation with the formation of the neural tube, which divides into three sections that give rise to the forebrain, midbrain, and hindbrain. A further division of the forebrain vesicle into the telencephalon and diencephalon occurs, from which the cerebral cortex and subcortical structures arise, respectively (Stern, 2001; Stiles & Jernigan, 2010). Following these divisions are cascades of cellular events that signal the beginning of neurogenesis at the subventricular zone around the fifth week. Neurons then differentiate and migrate to their designated position in the now-forming layers of the cortex (Stiles & Jernigan, 2010). This process takes place in an "inside-out" manner, with the oldest born neurons migrating to the outermost layer. Neuronal migration peaks between the 12th and 20th weeks of gestation (de Graaf-Peters & Hadders-Algra, 2006).

Synaptogenesis and Pruning

Following migration, neurons extend axons and dendrites to form connections to their synaptic partners. Studies in primates have shown that synapses begin to form shortly after neurogenesis and are continually remodeled thereafter, with peak refinement taking place largely after the 20th week and continuing into the perinatal period (Kostovic, Judas, Rados, & Hrabac, 2002). Brain systems develop at temporally distinct rates, with synaptogenesis reaching its most mature prenatal state in somatosensory regions earlier than in visual ones (Kostovic & Rakic, 1990). Dendritic arborization and synaptogenesis accelerate in the third trimester and by gestational Week 32, the cortex has adult-like laminar structure (Kostovic, Judas, Petanjek, & Simic, 1995). In Week 34, synaptogenesis peaks, with 40,000 new synapses formed every second—a process that continues into postnatal life (Rakic, Bourgeois, & Goldman-Rakic, 1994). To balance with the overproduction of synapses, pruning occurs via apoptosis to cull unnecessary or incorrect connections (Rakic & Zecevic, 2000). Studies in human cortex find rapid development of

synapses, dendritic spines, and dendritic tree complexity that peaks in the first few years of life (Huttenlocher & Dabholkar, 1997; Petanjek, Judas, Kostovic, & Uylings, 2008; Petanjek et al., 2011).

Myelination

Once neurons are positioned in the cortex and have sent out their local connections via dendritic trees, they extend long-range axons that form fiber bundles connecting different cortical and subcortical regions. These axons will later be wrapped in a lipophilic substance called "myelin" to form the white matter of brain (Stiles & Jernigan, 2010; Dubois et al., 2014). Myelination is a crucial process for the enhancement of neural signaling, because myelin is an electrical insulator that allows for fast information transfer between neurons. Myelination begins during Week 28 and follows an inside-out, back-to-front manner, such that subcortical regions myelinate first (Brody, Kinney, Kloman, & Gilles, 1987). At birth, relatively few axons are sheathed in myelin; thus, most of this process occurs in the first years of life. White matter maturation is largely concurrent with experience-dependent plasticity and learning (Dubois et al., 2014).

Brain Development during Early Life

In the early postnatal period, glial proliferation, axonal formation, and dendritic arborization result in dramatic increases in brain volume and cortical surface area, while synaptic pruning acts to regulate these processes (Gilmore, Lin, Corouge, et al., 2007; Knickmeyer et al., 2008; Lyall et al., 2015). Concurrently, but much more slowly, myelination results in an increase of white matter volume and a maturation of microstructural integrity along tracts (Knickmeyer et al., 2008; Geng, Gouttard, et al., 2012). The development of gray and white matter via synaptogenesis, pruning, synaptic remodeling, and myelination are fundamental to establishing neural circuits. We discuss how these specific processes contribute to shaping brain development in the preschool period following a critical introduction to magnetic resonance imaging and its uses for the *in vivo* study of the human brain.

IMAGING EARLY BRAIN DEVELOPMENT

Magnetic resonance imaging (MRI) has vastly increased our understanding of the living human brain through its applications for studying cortical and subcortical structures via structural MRI (sMRI), white matter tractography via diffusion tensor imaging (DTI), and brain functional activation and connectivity via functional MRI (fMRI). MRI has become increasingly popular for studying trajectories of human brain development, because it poses no medical threat and provides unparalleled access to the human brain *in vivo*.

Principles of MRI

MRI is based on the principles of nuclear magnetic resonance (NMR), which relies on atomic nuclei having different physical properties that can be identified analytically. MRI capitalizes on this concept and uses different magnetic frequencies to disrupt nuclei, causing naturally spinning protons to align with the magnetic field. These protons can then be knocked out of alignment by a second, short magnetic pulse; the rate at which they realign to the magnetic field differs based on the local environment of the proton (i.e., the rate differs based on the type of tissue in which the proton resides). MRI can distinguish between the brain's two main tissue types: gray matter (GM) and white matter (WM), and cerebrospinal fluid (CSF). The intensity of GM, WM, and CSF is largely dependent on the acquisition parameters of the MRI, and this principle can be helpful in assessing brain structure (see different examples of MRIs across early development in Figure 3.1).

sMRI

sMRI uses different image types (T1, T2; Figure 3.1) to delineate GM containing cell bodies, glia, and unmyelinated connections from WM containing myelinated (or premyelinated) axons (Prastawa, Gilmore, Lin, & Gerig, 2005; Zatorre, Fields, & Johansen-Berg, 2012). Differentiating these two tissue types can give us great insight into how the brain is structured and is useful for analyzing the cortical surface, the WM skeleton, and subcortical nuclei. The longest-standing image analysis technique for sMRI is the generation of brain volumes, beginning with the calculation of CSF volumes in the

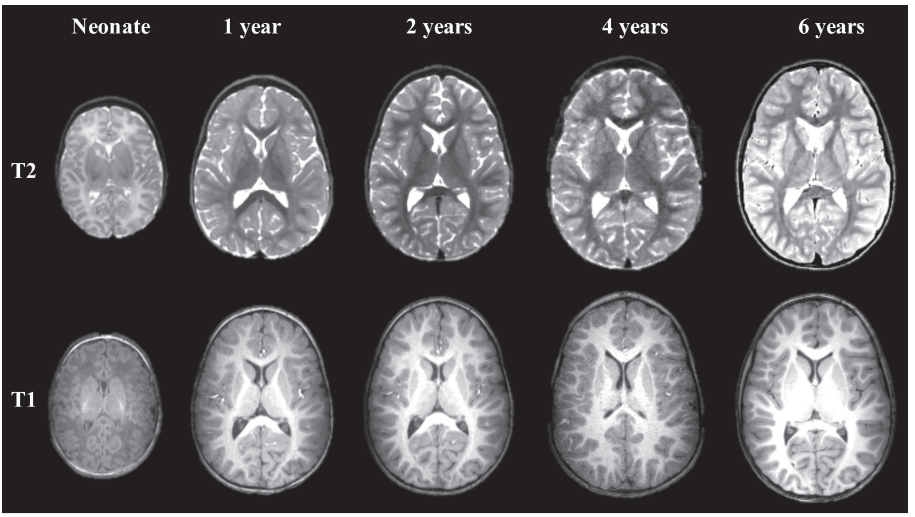

FIGURE 3.1. Structural MRIs of the brain from birth to 6 years.

1980s (Condon et al., 1986). This requires segmenting the brain into tissue types based on their intensity and calculating the amount of each tissue in the entire brain (global volumes), or in a specific region of interest (ROI) within the brain. These volumes reflect the number of three-dimensional (3-D) pixels (voxels) within the image that match the contrast intensity of each tissue type. Voxels are typically 1 mm^3–2 mm^3 and can contain anywhere from several thousand to tens of thousands of neurons (Lenroot & Giedd, 2006). In a postmortem study, Schumann and Nordahl (2011) found that there were ~7,000 neurons/mm^3 in the amygdala and ~40,000 neurons/mm^3 in the cortex of a 3-year-old human brain. This highlights that human neuroimaging, while reflective of underlying neural mechanisms, has limited ability to reveal information at the microscopic level. In addition to volumetric analyses, the field has advanced to examining the cortical surface through 3-D reconstructions. This can involve measuring cortical surface area, thickness, and gyrification (Li et al., 2014; Lyall et al., 2015). sMRI can also be used to study the size and shape morphometry of subcortical nuclei and lateral ventricles (Styner, Gerig, Lieberman, Jones, & Weinberger, 2003).

Diffusion Tensor MRI

DTI is a powerful MRI technique for the visualization and characterization of WM in the brain. DTI capitalizes on the principles of diffusion and the fact that water diffuses differently in GM and CSF than in WM. In CSF and among cell bodies in GM, water is allowed to diffuse freely in an isotropic manner. However, axons coated in myelin restrict diffusion of water along a principal direction, creating anisotropic diffusion. DTI can capture measures of both the degree and directionality of diffusion. The degree of diffusion (usually indexed by a measured called "fractional anisotropy" [FA]) describes the microstructure of the WM bundles; for example, higher values of FA reflect higher degrees of myelination; Feldman et al., 2010). Understanding the directionality of the water diffusion is critical for fiber tract reconstruction, which allows us to probe different anatomical and functional pathways in the brain. While powerful, DTI has limitations in its ability to resolve crossing fibers and therefore to track with the same anatomical precision as tracer studies in postmortem tissue (Qiu, Mori, & Miller, 2015). Interpretations of DTI results may also undermine the importance of water in other biological mechanisms such as membrane and protein dynamics (Thomas et al., 2014; Qiu et al., 2015).

fMRI

fMRI is used to detect changes in the blood-oxygen-level-dependent (BOLD) signal generated by an increase in deoxygenated blood (which has a different magnetic signal than tissue or arterial blood) following neural activation (Gore, 2003). fMRI can be combined with cognitive and behavioral assessments to measure how the brain performs tasks or responds to particular

stimuli, typically referred to as "task-based fMRI." The brain can also be studied at rest ("resting-state fMRI"), which means that no stimuli are used to evoke responses, but neuronal activity is still present and synchrony can be observed between connected brain regions (Biswal, Yetkin, Haughton, & Hyde, 1995). Coordinated activity reveals large-scale neural networks that can be extracted during resting-state or task-based fMRI and provide insight into how the brain functions (Bullmore & Sporns, 2009). fMRI has limitations, including a lag in temporal resolution and the inability to distinguish between excitatory or inhibitory activation (Gore, 2003). Head motion can influence resting-state fMRI results, and it is necessary to correct for motion (Power, Schlaggar, & Petersen, 2015).

Imaging the Brain during Early Development

Neuroimaging studies of infants and young children have inherent challenges and limitations. Subject cooperation and movement in the scanner, as well as the need to collect data while sleeping in very young children, prove difficult in a practical sense. Image analysis during this period also has unique challenges, including low contrast-to-noise ratio, contrast changes and intensity inhomogeneity due to myelination, small and variable size of anatomical shapes, and rapid changes in morphology over time (Prastawa et al., 2005). Despite these technical limitations, MRI has proved to be an invaluable tool for studying human brain development.

TRAJECTORIES OF BRAIN DEVELOPMENT IN THE PRESCHOOL PERIOD

Brain maturation during the preschool period is marked by dynamic and expansive anatomical and functional growth. The brain experiences its most rapid period of growth in the first 2 years of life, doubling in size during the first year and reaching 80% of adult volume by the second year (Knickmeyer et al., 2008). The brain continues to grow and reshape itself at a slower rate from ages 2–6 years, when it has obtained 90% of its adult volume (Lenroot & Giedd, 2006). This growth is the result of many complex mechanisms that contribute to the development of the cortex, subcortical nuclei, and WM pathways that lay the foundations that will be built upon and remodeled via mechanisms of plasticity and learning throughout the lifespan.

The Developing Cortex

The volume of the cortex nearly doubles in the first year of life, and the majority of this growth is driven by the expansion of GM which likely reflects underlying dendritic arborization, axonal elongation and remodeling, and glial proliferation (Gilmore, Lin, Prastawa, et al., 2007; Gilmore et al., 2012;

Knickmeyer et al., 2008). The second year of life shows more modest growth, with cortical GM volume increasing around 18% (see Figure 3.2; Gilmore et al., 2012). The cortex also exhibits regionalized differences in volumetric growth rates, with primary motor and sensory cortices growing slower in the first year of life than association cortices, a pattern that continues into the second year (Gilmore et al., 2012). Studies of cortical thickness (CT) and surface area (SA) have shown that this volumetric increase in GM in the first few years of life is primarily driven by SA expansion, which doubles from birth to 2 years of age (Lyall et al., 2015).

At birth the primary sensory and motor cortices are the thinnest, while thicker regions include the association cortices related to higher-order functioning. These patterns are generally stable throughout the first 2 years, with thinner regions growing more slowly than thicker regions in the first year (average increase of 30%), and less overall growth taking place in the second year (5% increase), when the cortex has reached 97% of adult thickness values (see Figure 3.3; Li et al., 2014; Lyall et al., 2015). Studies of children ages 5–11 showed thinning across large areas of the cortex and a low rate of thickening in Broca's and Wernicke's areas, which are important for language development (Sowell et al., 2004). Recent studies of children (4 years and older) and adults show that CT decreases across the lifespan at steady rates (Brown & Jernigan, 2012; Amlien et al., 2016). This highlights that CT develops fastest

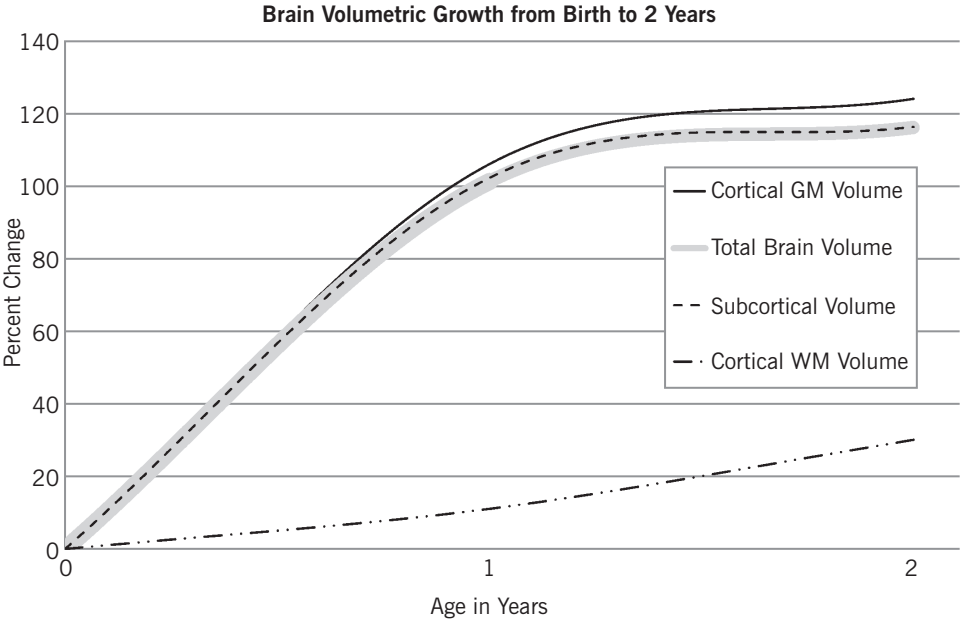

FIGURE 3.2. Brain volumetric growth from birth to 2 years.

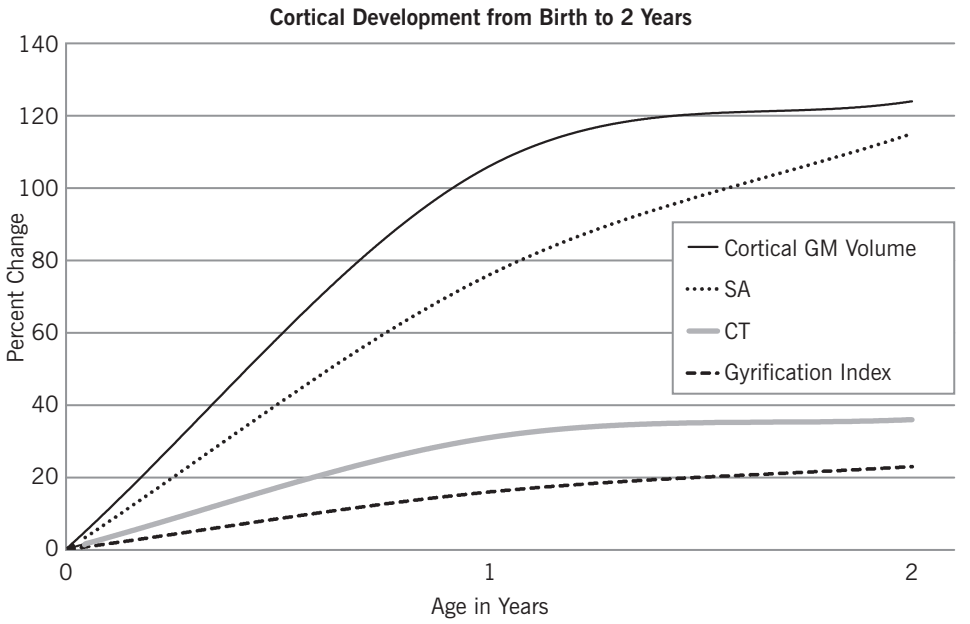

FIGURE 3.3. Cortical development from birth to 2 years.

in the first years of life, and that this period may uniquely exhibit rapid thickening.

SA expansion does not follow the same patterning as CT and it also develops at different rates, in line with research showing that these two components of cortical structure are genetically distinct (Panizzon et al., 2009; Chen et al., 2013; Lyall et al., 2015). The expansion of the cortex is regionally heterogeneous, with growth rates from birth to 2 years ranging from 7 to 150%; the fastest growing regions are sensory-specific association cortices (Figure 3.3; Lyall et al., 2015). Rapid growth of visual, auditory, and sensorimotor cortices may be related to the expansion of topographic maps from sensory input and experience. SA exhibits its fastest period of growth in the first 2 years of life; by age 2 it has reached 69% of adult values (Lyall et al., 2015), and continues to grow slowly until it peaks around age 12, then declines thereafter (Raznahan et al., 2011; Amlien et al., 2016). This suggests that postnatally, the first 2 years mark a critical period for the regulation of cortical and total brain size—an idea supported by studies of children with autism spectrum disorder who exhibit increased SA before age 2 (Hazlett et al., 2011).

To allow for the drastic increase in SA relative to the skull, cortical gyrification increases in early development as well. Major cortical folding of gyri and sulci are present at birth, and only tertiary folding structures undergo

development after birth (Li et al., 2013). In the first year of life, cortical gyrification increases 16%, followed by 6% in the second year (Figure 3.3; Li et al., 2014). Regionalized differences in cortical gyrification are observed, with association areas being the highest, meaning they have the most cortex exposed to the outer surface (Li et al., 2014). The spatial location of sulci was found to be consistent across this developmental window and also related to overall brain volume, once again highlighting that cortical folding is an important mechanism for early brain growth (Meng, Li, Lin, Gilmore, & Shen, 2014).

Growth of Subcortical Nuclei

Subcortical maturation in the first years of life follows the same general growth pattern as the rest of the brain, with the largest increase in volume in the first year and a more modest level of growth thereafter (Utsunomiya, Takano, Okazaki, & Mitsudome, 1999; Gilmore et al., 2012; Raznahan et al., 2014). The majority of subcortical nuclei (amygdala, thalamus, caudate, putamen, pallidum) double in size in the first year, except for the hippocampus, which increases about 85% in volume (Figure 3.2; Gilmore et al., 2012). Findings from a sample of infants scanned from birth to 3 months of age recapitulate these findings, showing that the hippocampus grows most slowly (47% increase) when compared to other subcortical nuclei (52–66% increase) (Holland et al., 2014). Another study of children ages 3–13 months revealed that the putamen grows faster than the rate of overall brain growth during this period (Choe et al., 2013). Later studies show that from ages 5 to 25 years there is a gradual increase in subcortical volumes, which peak in during puberty (earlier in females than males), up to a few years after the peak in cortical volumes (Raznahan et al., 2014). These data suggest that subcortical nuclei grow rapidly in the first years of life and are later modified as part of the developmental process during adolescence.

Cerebellar Growth

The cerebellum is the fastest growing brain structure in the first 2 years of life, increasing 240% in volume from birth to 2 years of age (Figure 3.2; Knickmeyer et al., 2008). In the first 90 days alone, the cerebellum doubles in size (Holland et al., 2014), and shows accelerated growth beyond that of total brain growth from 3 to 13 months of age (Choe et al., 2013). Given the important role of the cerebellum in motor function, its dramatic growth may be required to facilitate rapid motor gains in early life.

WM Maturation

WM volume grows slightly over 10% in the first year of life and about 20% in the second (Figure 3.2; Knickmeyer et al., 2008); however, there is much

maturational change that is reflected not by volume growth but instead by changes in diffusion signal due to myelination and organization of axons. Postmortem studies have shown that myelination occurs rapidly from midgestation through the first 2 years of life and follows a strict topographical pattern, with myelination occurring in proximal before distal, sensory before motor, projection before association, and occipital before frontal fiber pathways (Brody et al., 1987).

Myelination increases most in the first year of life, reflected by fiber tracts exhibiting a 9–44% increase in anisotropic diffusion (indexed by FA), with the majority of tracts showing more than a 25% increase in FA (Figure 3.4; Gilmore, Lin, Corouge, et al., 2007; Geng et al., 2012). The second year shows a much lower increase in FA, ranging from 5 to 9% (Figure 3.4; Geng et al., 2012). More direct assessment of myelin content *in vivo* by studies of myelin water fraction (MWF) show that by 2.5 years, myelin content in the brain has reached 80% of adult values (Deoni, Dean, O'Muircheartaigh, Dirks, & Jerskey, 2012). At birth, callosal tracts connecting the hemispheres are less myelinated but have more organized axonal and fascicular structures than other tracts and also mature the fastest in the first 2 years. Projection tracts responsible for sensory and motor functions are the most myelinated and mature at birth, and mature at the slowest rate thereafter. Association

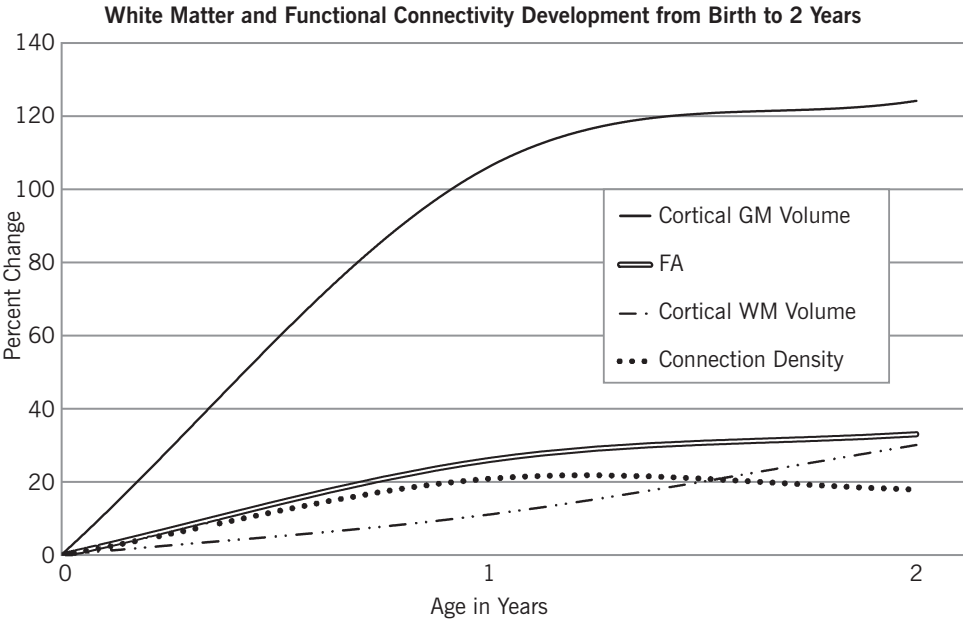

FIGURE 3.4. White matter and functional connectivity development from birth to 2 years.

tracts for higher-level integration (arcuate, uncinate, and inferior longitudinal fasciculus) are consistently lower in maturational state than other tracts from birth to 2 years of age (Geng et al., 2012). These results are in line with the early maturation of sensory and motor skills and the later development of higher-order processing (Qiu et al., 2015).

Functional Brain Development

The functional development of the human brain during the first 2 years of life is just as complex and dynamic as its structural development. Studies of resting-state functional connectivity networks in young children reveal that visual and sensorimotor networks are present at birth and mature rapidly in the first 2 years of life (Lin et al., 2008). In particular, it was shown that connectivity in sensorimotor cortices precedes that in the visual areas, and that percent of brain volume contributing to the signal increases with age (Lin et al., 2008). This work highlights both the temporal and spatial dynamics of functional brain development in early life, and is in line with the progression of synaptogenesis in the cortex (Kostovic & Rakic, 1990).

In addition to changes in cortical activity, the topology or "structure" of brain networks also develops in early life. From birth to 2 years, changes in topology are shown by a shift from immature, short-range connections at birth to adult-like, long-range connections that are important for efficient information transfer between anatomically distant regions (Gao, Gilmore, et al., 2011; Di Martino, Fair, et al., 2014). This maturation is reflected by an increase in density of longer connections from 25% at birth to 46% in the first year and roughly the same in the second (Figure 3.4; Gao et al., 2011). Interestingly, there are different hubs (connection centers) in early life than in adulthood. While adults have hubs in higher-order processing regions such as the prefrontal and medial-parietal regions, neonates and infants show hubs in regions more associated with motor and visual skills (Gao et al., 2011). Studies in older children (ages 7–9 years) reveal that there are still stark contrasts in brain network architecture between children and adults, which is in agreement with the prolonged maturation of higher-order cognitive systems (Fair et al., 2008).

Studies of canonical brain networks in infants and young children reveal interesting patterns of development. The default mode network (DMN)—present during rest and representative of undirected mental states—comprises functional synchrony between the posterior cingulate cortex (PCC), medial prefrontal cortex (mPFC), lateral temporal cortex (LTC) and inferior parietal lobule (IPL), and has been related to behavioral performance and emotional measures (Greicius, 2008). At birth the DMN is incomplete and primitive in nature, but it then expands in both space and connectivity strength during the first year of life, and by age 2 it is largely similar to that observed in adults (Gao, Zhu, et al., 2009). During this age range, we see that the PCC portion of the network is the strongest, and may be the main hub of the network from a developmental standpoint (Gao, Zhu, et al., 2009).

Dorsal attention networks follow a similar pattern of development, expanding from an immature network at birth to a more adult-like network by 2 years of age (Gao et al., 2013). This improvement in overall network integration occurs most rapidly in the first year and coincides with the functional specialization of the default and dorsal attention networks. Specifically, in neonates, the hub regions between the two networks are largely overlapped, but this spatial overlap is significantly reduced at 1 year of age and nearly vanishes by age 2 (Gao et al., 2013). This suggests that networks at birth interact and house similar functions but become progressively specialized to their specific roles through experience and learning.

THE GENETICS OF EARLY BRAIN DEVELOPMENT

Technological advances in genetics, genomics, and neuroimaging are providing new insights into how genetic variation impacts brain structure and function (Thompson, Ge, Glahn, Jahanshad, & Nichols, 2013; Strike et al., 2015). At present, the vast majority of this research has been conducted in adolescents and adults, but there is a growing body of literature addressing this critical issue in infants and young children. In this section we review recent work using transcriptomics, classical twin methods, and the candidate gene approach.

Regarding transcriptomics, the majority of protein-coding genes show marked differences in expression over the course of neurodevelopment. Temporal gradients are strong during the fetal period; moderate during infancy, childhood, and adolescence; and extremely rare during adulthood and aging (Kang et al., 2011). Prenatal cortical development is characterized by robust regional differences in gene expression, while infancy and early childhood are characterized by minimal regional differences. This shift likely reflects differences in maturational processes across prenatal and postnatal development. Genes expressed in the fetal brain show an enrichment of transcription factors (Zhang, Landback, Vibranovski, & Long, 2011) and are likely critical for the establishment of area-specific subcortical and cortico-cortical projections. In contrast, genes controlling dendritic development, synaptogenesis, and myelination dominate the early postnatal period (Pletikos et al., 2014), processes that are active in the cortex and strongly influenced by experience and social input.

The classical twin design compares the similarity of monozygotic (identical) and dizygotic (fraternal) twins and uses this to estimate the proportion of phenotypic variance attributable to genetics (heritability) versus shared and unique environments. In neonates, heritability is high for intracranial volume (ICV), total WM, and lateral ventricle volume; moderate for total GM; and low for cerebellar volume. Comparisons to studies of older children and adults suggest the heritability of global GM and cerebellar volume increases with age, while the heritability of lateral ventricle volume decreases with age

(Gilmore, Schmitt, et al., 2010). DTI studies of neonatal WM have found significant genetic influences on global, regional, and tract-based diffusion properties (Geng et al., 2012; Lee et al., 2015), with variability in heritability between regions and along and between tracts. Heritability also appears to decrease with age in the neonatal period, suggesting an important role for environmental factors in shaping individual differences in WM maturation and integrity. Genetic influences on functional connectivity have also been reported in infancy (Gao et al., 2014).

Candidate gene studies test whether variants in prespecified genes of interest are associated with particular phenotypes (in this case, neuroimaging measures). Genes are selected based on biological plausibility and functional relevance. Our group produced the first report that putative risk genes for Alzheimer's disease (AD) and mental illness predicted local GM volumes at birth (Knickmeyer et al., 2014a). Significant associations were also identified for variants in *DISC1, COMT, NRG1, APOE, ESR1,* and *BDNF*. Subsequently, Dean et al. (2014) studied the impact of variation in *APOE* on myelin water fraction (an index of myelination) and GM volumes in the first 2 years of life. Both studies report that carriers of the e4 variant (a major risk factor for AD) exhibit altered brain structure in regions relevant to AD during infancy, indicating that risk genes for adult-onset disorders have altered infant brain structure by birth.

While the candidate gene approach continues to be a powerful method for elucidating how genetic variants of known clinical relevance impact brain structure and function, future research is expected to shift toward genome-wide association studies (GWAS). GWAS is an agnostic approach that scans millions of markers across the genomes of many people to find novel variants associated with phenotypes of interest. GWAS of neuroimaging data collected in adolescents and adults have identified 19 genetic variants for brain structure, though no replicated associations account for more than 1% of the variance (Strike et al., 2015). GWAS in infants and young children may better capture individual differences in early neurodevelopmental processes, including cell differentiation and growth, neuronal migration, dendritic arborization, synaptogenesis, myelination, programmed cell death, and synaptic pruning.

ENVIRONMENTAL INFLUENCES ON BRAIN DEVELOPMENT

While genetic differences play an important role, twin studies demonstrate that environmental factors account for a substantial portion of interindividual variance in brain structure during infancy (Gilmore, Kang, et al., 2010). The so-called "envirome" encompasses an almost infinite variety of exposures (Anthony, 2001), but within this vast search space, prenatal and early postnatal influences are likely of particular importance. In this section we briefly

review the published literature on prematurity; socioeconomic factors; and prenatal exposure to alcohol, maternal smoking, and illicit drugs.

Regarding prematurity, WM abnormalities represent the most common pathology seen in preterm infants using MRI. This includes cystic lesions, punctate lesions, delayed myelination, volume loss, thinning of the corpus callosum, and T2-weighted diffuse excessive high signal intensity (DEHSI). Widespread alterations in WM integrity as assessed by DTI have also been frequently reported (Anderson, Cheong, & Thompson, 2015). Even in infants without focal brain lesions, global reductions in cortical and subcortical GM and brain stem volumes, and increases in CSF volumes are observed at term equivalent age (Padilla, Alexandrou, Blennow, Lagercrantz, & Aden, 2015). Early deficits are partially compensated for by accelerated brain growth in infancy (Holland et al., 2014), but reduced GM volumes are still observed in adolescence (de Kieviet, Zoetebier, van Elburg, Vermeulen, & Oosterlaan, 2012). Reductions in resting network connectivity have also been reported in very preterm infants without brain injury (Smyser et al., 2016). Neuroimaging parameters are predictive of neurodevelopmental outcomes, though results must be interpreted in conjunction with other clinical and social information (Anderson et al., 2015).

Disparities in socioeconomic status (SES) predict cognitive performance and language development in the first 2 years of life (Noble, Engelhardt, et al., 2015). These differences have not been directly linked to brain morphology, but children from low-income households display slower trajectories of GM growth during later infancy and early childhood (Hanson et al., 2013). A low income-to-needs ratio continues to be associated with reduced cortical GM and WM volumes in school-age children (Luby et al., 2013) and family income is positively associated with cortical SA into adolescence (Noble, Houston, et al., 2015). These associations likely arise through multiple factors, including access to and utilization of prenatal care; postnatal levels of cognitive and psychosocial stimulation; availability of nutritious food; and exposure to stress, trauma, infections, and environmental toxins.

Prenatal exposure to alcohol, nicotine, and illicit drugs is often associated with low birthweight, premature delivery, and short- and long-term behavioral abnormalities in offspring. The most common neuroimaging findings in children exposed prenatally to alcohol are reduced brain volumes and malformations of the corpus callosum (Lebel, Roussotte, & Sowell, 2011). Altered diffusion along WM tracts and abnormalities on fMRI have also been reported (Roussotte, Soderberg, & Sowell, 2010). Current studies are largely restricted to children above 4 years of age. Additional complementary studies in infants are needed to develop effective strategies for early risk identification and intervention.

Similarly, there are no volumetric studies on smoking exposure in full-term, newborn infants, but frontal lobe and cerebellar volumes are significantly smaller in preterm infants exposed to maternal smoking compared to unexposed preterm infants. In adolescents, prenatal smoking exposure is

associated with thinner frontal, temporal, and parietal lobes and smaller cortical GM and corpus callosum volumes. Alterations in WM integrity and a lack of coordination across brain regions during information and auditory processing have also been reported (Ekblad, Korkeila, & Lehtonen, 2015).

Infants with prenatal cocaine exposure show GM reductions in prefrontal and frontal regions involved in executive function and inhibitory control (Grewen et al., 2014). Infants with polydrug exposure (e.g., nicotine, alcohol, marijuana, and antidepressants) show disrupted functional connectivity within amygdala–frontal, insula–frontal, and insula–sensorimotor circuits. Moreover, a cocaine-specific effect was detected within a subregion of the amygdala–frontal network involved in arousal regulation (Salzwedel et al., 2015).

SEX DIFFERENCES IN THE DEVELOPING BRAIN

There are numerous reports of sexual dimorphism in brain structure in children and adults, but data on sex differences in infancy, until recently, were extremely limited. Our group produced the first detailed information on sex differences in global, regional, and local brain volumes in the neonate and the effects of androgen exposure and sensitivity on brain structure in this critical period (Knickmeyer et al., 2014b). There was a significant sex difference of 5.87% for intracranial volume that was not related to androgen exposure or sensitivity. The magnitude of this difference was smaller than that reported in children (De Bellis et al., 2001) and adults (Gur et al., 1999; Nopoulos, Flaum, O'Leary, & Andreasen, 2000), which suggests that males experience accelerated brain growth in the first several years of life when compared to females. This hypothesis is supported by our recent study on longitudinal development of CT and SA, in which we observed that males had a significantly faster rates of SA expansion compared with females in several cortical regions, including the left precentral gyrus, superior frontal gyrus, middle frontal gyrus, olfactory gyrus, insula, superior parietal gyrus, and right calcarine gyrus (Lyall et al., 2015). Tensor-based morphometry in the neonate identified extensive areas of local sexual dimorphism. Males had larger volumes in medial temporal cortex and Rolandic operculum, and females had larger volumes in dorsolateral prefrontal, motor, and visual cortex. Androgen exposure and sensitivity had minor sex-specific effects on local GM volume but did not appear to be the primary determinant of sexual dimorphism at this age (Knickmeyer et al., 2014b).

We have also reported on gender differences in cortical global gyrification index (GI) and local gyrification index (LGI) during the first 2 years of life. We observed that males had a larger GI at 2 years of age (adjusting for total brain volume) but not at birth or 1 year of age. LGI was substantially similar between males and females at all ages (Li et al., 2014). Cortical folding during early postnatal development may serve as a marker of later neurobehavioral

development, although the molecular and mechanical mechanisms responsible for postnatal development of GI and LGI are not fully understood (Zilles, Palomero-Gallagher, & Amunts, 2013).

Comparing our studies to the existing literature indicates that sex differences in cortical structure vary in a complex and highly dynamic way across the human lifespan. Sexual dimorphism of the brain likely emerges via the dynamic interplay of multiple mechanisms both biological (e.g., gonadal steroid exposure and direct sex chromosome effects) and experiential (e.g., parental expectations and interactive behavior, exposure to physical hazards, and culturally influenced lifestyle differences) (Rutter, Caspi, & Moffitt, 2003). Longitudinal designs accounting for multiple factors are needed to understand fully the relationship between sex differences in brain development, cognitive function, and behavioral outcomes in early life.

BRAIN DEVELOPMENT AND COGNITION

The progression of brain development in the first years of life is in line with the maturation of sensory, motor, and cognitive skills, though there has been very little research investigating exactly how the brain matures to support normal adaptation and cognitive growth. Even less investigated are the trajectories of brain development between healthy children of different ability, which would lend insights into the variability within typical development and how that relates to cognitive outcomes. It has been well established in older children and adults that changes in brain structure over time are related to cognitive ability (Shaw et al., 2006; Erus et al., 2015); thus, linking early brain development to cognition will create a larger perspective on the lifespan development of brain structure–function relationships.

The majority of research on infant brain structure and cognition comes from studies of prematurely born infants. This body of research highlights two main points: (1) Premature children have less developed brains a birth and often show signs of cognitive delays in early life, and (2) early brain structure can be predictive of later cognitive outcomes (Peterson et al., 2000; Anderson et al., 2015). More recent work in typically developing children supports the predictive ability of early brain structure and maturational profiles for general cognitive ability (Deoni et al., 2014; O'Muircheartaigh et al., 2014). Interestingly, differences in the maturational profiles of WM in the first few years of life were seen between children who score above, at, and below average on the Mullen Scales of Early Learning (Deoni et al., 2014; O'Muircheartaigh et al., 2014). Another study showed WM tracts associated with working memory in adults were also related to working memory scores in 1-year-olds, even after researchers controlled for general developmental level (Short et al., 2013). Thalamocortical connectivity is also related to working memory at both 1 and 2 years of age, indicating an important role for sensory–integration networks in early cognition (Alcauter et al., 2014).

Cognitive development, like brain development, is an ongoing process that begins at birth and continues throughout the lifespan. Cognitive development involves the reshaping and fine-tuning of cortical circuits as part of neuroplastic responses to environmental input and experience. The maturation of cognitive skills aligns with the development of brain systems, in which sensory and motor processes develop first, followed by association functions and top-down control of executive functions (Casey, Tottenham, Litton, & Durston, 2005). Future studies seeking to identify brain–behavior relationships and trajectories will need to employ longitudinal modeling techniques that identify critical periods in brain and cognitive development.

IDENTIFYING ABERRANT DEVELOPMENT IN HIGH-RISK POPULATIONS

Studying the neurobiological origins of psychiatric and developmental disorders is of utmost interest to clinicians and scientists alike. Recently, particular focus has been placed on studying children who are at high risk for developing these disorders but have yet to show symptoms. Targeting and following at-risk populations is useful for identifying biological mechanisms that give rise to phenotypic traits before treatments (by pharmaceuticals and other methods of intervention) have had a chance to alter physiology. Much of this type of high-risk research related to neurodevelopmental disorders has been conducted in infants and children at risk for developing an autism spectrum disorder (ASD) and schizophrenia (SCZ). In both disorders, there are genetic and environmental components, and those considered at-risk will have a first-degree relative (mother, father, sibling) with clinical symptomatology (McGuffin et al., 1984; Hallmayer et al., 2011). One difference between SCZ and ASD is the timing of symptom presentation: ASD often presents in the preschool period, whereas SCZ is not typically diagnosed until the teenage years or later. In SCZ and ASD, there is evidence of heterogeneous behavioral abnormalities and cognitive disabilities very early in life (Trevarthen, 2000; Shaw, Gogtay, & Rapoport, 2010; Rapoport & Gogtay, 2011), when the foundations of neural circuits are forming and aberrant development may lead to a "miswiring" of the brain.

Research on children at risk for developing ASD has yielded much evidence in the last decade. Some of the most prominent findings include cerebral enlargement in early childhood (Hazlett et al., 2011; Shen et al., 2013) and atypical development of functional and structural connectivity (Wolff et al., 2012). Additional differences include cortical structure, corpus callosum morphology, and extra-axial CSF volumes (Hazlett et al., 2011; Shen et al., 2013; Wolff et al., 2015). These differences in early brain development occur between control groups, children at risk who do not develop ASD, and those who have risk and do develop ASD—providing insight into how risk can convert to either clinical diagnosis or subclinical symptomatology.

Differences in these developmental trajectories can be observed as early as 6 months of age using both neuroimaging and cognitive assessments (Wolff et al., 2015).

Studies of infants of mothers with SCZ have also produced insights into the perinatal and early life abnormalities present in these high-risk offspring. Our group presented the first evidence that neonatal brain structure may be abnormal in males at risk for SCZ (Gilmore, Kang, et al., 2010); this study found that male offspring of mothers with SCZ had larger than normal GM, CSF, and lateral ventricle volumes when compared to controls. Interestingly, at-risk female offspring did not differ from healthy subjects. High-risk male offspring also show a more disconnected phenotype, with altered GM and WM connectivity at birth (Shi et al., 2012). Cortical structure may also be altered in high-risk neonates (Li, Wang, Shi, Lyall, Ahn, et al., 2016). Studies of childhood-onset SCZ (COS; defined as having a clinical diagnosis before age 13) indicate that subjects with COS have distinct neurodevelopmental trajectories marked by progressive loss of GM, delayed and disrupted WM maturation, and a progressive decline in cerebellar volume from around age 7 into the teenage years (Rapoport & Gogtay, 2011).

Developmental trajectory research holds the key to understanding when, where, and how alterations in brain maturation occur and contribute to changes in phenotypic outcomes. It is likely that the variety of existing neurodevelopmental disorders is produced by a vast array of deviations from normal trajectories of growth. While some disorders may reflect a delay or acceleration in neurodevelopmental processes, others may show a halting of the process altogether or, worse yet, a complete "derailment" from normality (Shaw et al., 2010).

CONCLUSIONS AND FUTURE ENDEAVORS

The first 2 years of life mark the most rapid phase of human brain development. Developmental trajectories during this time are sexually dimorphic, genetically controlled and heritable, influenced by early life exposures, and play an important role in determining cognitive and neurodevelopmental outcomes. Studying this type of complex process requires the use of longitudinal study designs and the collection of vast amounts of neuroimaging, genetic, cognitive, behavioral, and demographic data. Results from these types of studies in the past decade have revealed great insights into human brain development.

At birth, the brain is comprised of a layered, folded cortex that matures to an adult-like state in the first years of life. By age 2, the cortex has reached 70% of adult area, 97% adult thickness, 80% of adult volume, and exhibits adult-like patterns of WM microstructure and functional connectivity. This development ensures that the foundations of brain circuitry required for

learning are in place by the end of the second year. The substantial amount of growth exhibited in the first 2 years of life identifies it as a critical period for the developmental of normal brain circuitry and function; thus, aberrant development during this time may have severe consequences. Future research in the field of neuroscience will continue to investigate neurodevelopmental processes that give rise to cognition and behavior in healthy children and those at risk for neurodevelopmental disorders.

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Part II

Behavioral and Emotional Disorders in Preschool Children

4

Oppositional Defiant Disorder and Conduct Disorder

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Clinicians have long been reluctant to diagnose young children with oppositional defiant disorder (ODD) and conduct disorder (CD). The question has indeed been raised as to how one differentiates clinical from normative transient disruptive behaviors within the preschool period, because most preschoolers exhibit at least some of the behaviors that fall under the rubric of disruptive behavior (Wakschlag et al., 2005). In connection with this, a point of concern is the possibility of overidentification of preschool children as having ODD or CD (Keenan et al., 2007). Clearly, diagnosing a young child with, for example, ODD comorbid with attention-deficit/hyperactivity disorder (ADHD), and starting pharmacotherapy in the absence of these disorders is inappropriate (Bunte, Laschen, et al., 2013). On the other hand, diagnosing a preschool child with ODD or CD, with or without ADHD, is important in view of starting appropriate treatment needed to prevent the negative consequences of these disorders on the child's emotional, cognitive, and social development. Fortunately, in the last decade, assessment procedures have been developed with established reliability and validity, which also apply at an individual level. Likewise, it has been shown that interventions such as behavioral parent training and pharmacotherapy can affect symptoms of these disorders (Greenhill et al., 2006; Menting, Orobio de Castro, & Matthys, 2013).

This chapter is divided into six major sections: (1) diagnosis, (2) prevalence and comorbidity, (3) course, (4) etiology, (5) clinical assessment, and (6) treatment. Throughout the chapter, we review studies and discuss clinical

issues related to preschool children, but also include knowledge about ODD and CD in older children and adolescents.

DIAGNOSIS

In DSM-5 (American Psychiatric Association, 2013), ODD is defined as a pattern of angry/irritable mood, argumentative/defiant behavior, or vindictiveness lasting at least 6 months, as evidenced by at least four symptoms. These symptoms are exhibited during interaction with at least one individual who is not a sibling. The persistence and frequency of the symptoms should exceed what is normative for the individual's age, gender, and culture. For children younger than age 5 years, the behavior should occur on most days, whereas for children 5 years and older, the behavior should occur at least once a week. However, for the vindictiveness symptom, it is specified that the behavior must have occurred at least twice in the past 6 months. Researchers have agreed that symptoms of negative mood and affective dysregulation (angry/irritable mood) can be distinguished from symptoms of headstrong, antagonistic, and oppositional behavior (argumentative/defiant behavior) (Rowe, Costello, Angold, Copeland, & Maughan, 2010), whereas they disagree as to whether being spiteful (vindictiveness) loads on the behavioral dimension or not (Rowe et al., 2010; Stringaris & Goodman, 2009a).

A study of preschool children examined various dimensional models of ODD: the DSM-IV (American Psychiatric Association, 1994) single-factor model, a two-factor model (oppositional behavior, negative affect), and two three-factor models (one with dimensions of oppositional behavior, negative affect, and antagonistic behavior; a second with dimensions of irritability, and hurtful and headstrong). The two-factor model showed the best fit. The authors conclude that in young children, ODD is best characterized as two separate dimensions, one behavioral and one affective, which are comparable for both boys and girls in these age groups (Lavigne, Bryant, Hoplins, & Gouze, 2015). Based on the heterogeneity of symptoms, ODD may be considered a mixed disorder of behavior and emotion (Matthys, Vanderschuren, Schutter, & Lochman, 2012; Matthys, Vanderschuren, & Schutter, 2013), a characteristic to which both clinicians and researchers need to pay more attention.

In DSM-5, CD is defined as a repetitive and persistent pattern of behavior in which the basic rights of others or major age-appropriate societal norms or rules are violated, as evidenced by at least three symptoms in the past 12 months, with at least one symptom in the past 6 months. Four groups of symptoms are distinguished: (1) aggression toward people and animals, (2) destruction of property, (3) deceitfulness or theft, and (4) serious violations of rules. Some of the symptoms of CD, however, are not within the capacity of preschool children to perform, such as forcible sexual activity, use of weapons, and breaking into houses (Wakschlag, Leventhal, Thomas, & Pine, 2007).

Compared with DSM-IV, in DSM-5, the specifier "limited prosocial

emotions" is added. To qualify for this specifier, the child must display at least two of the four characteristics persistently over at least 12 months and in multiple relationships and settings: lack of remorse or guilt, callous–lack of empathy, unconcerned about performance, and shallow or deficient affect. These characteristics have been extensively studied in older children and adolescents as callous–unemotional traits (for a review, see Frick, Ray, Thornton, & Kahn, 2014). Callous–unemotional traits constitute the affective factor of psychopathy and designate a particularly aggressive subgroup of children and adolescents with antisocial behavior (Frick et al., 2014). Among children and adolescents with antisocial behavior, those with high levels of callous–unemotional traits display more instrumental aggression and show a more stable pattern of antisocial behavior (Frick et al., 2014). There is emergent evidence that low concern and callousness are evident at preschool age and have predictive utility for conduct problems (Ezpeleta, de la Osa, Granero, Penelo, & Domenech, 2013).

PREVALENCE AND COMORBIDITY

Few epidemiological studies of disorders in preschool children using community samples have been conducted. Egger and Angold (2006) reviewed research on the rate of disorders in preschool children. Studies showed a fairly wide range of prevalence estimates for ODD (4.0–16.8%) and CD (0–6.6%); these authors concluded that the prevalence rates of ODD and CD in preschool children are similar to those found later in childhood. However, the representativeness of the samples included in the review by Egger and Angold has been questioned by Wichstrøm and colleagues (2012) because the studies included used preschool program and pediatric samples. In a Norwegian community sample, on the other hand, the prevalence of ODD was 1.8% and that of CD was 0.7% (Wichstrøm et al., 2012). The lower prevalence of these and other disorders in Norway than in the United States may also be due to the relatively low rate of poverty and unemployment in Norway. Prevalence rates in another European community and in an American community sample are higher. In a Spanish community sample, the prevalence of ODD was 6.9% and of CD was 1.4% (Ezpeleta, de la Osa, & Domenech, 2014), and in a U.S. community sample the prevalence of ODD was 9.4 % (Bufferd, Dougherty, Carlson, & Klein, 2011).

Similar to its prevalence in older children, comorbidity is common in preschool-age children (Egger & Angold, 2006). Studies in young children have identified associations between ODD or CD and ADHD (i.e., homotypic comorbidity) and between ODD and depression or anxiety (i.e., heterotypic comorbidity) (Egger & Angold, 2006; Bufferd et al., 2011; Ezpeleta et al., 2014; Wichstrøm et al., 2012). Thus, clinicians should pay attention to the presence of comorbidity in the assessment and treatment of preschool children with ODD and CD.

COURSE

Evidence for the stability of ODD diagnosis in preschool children is critical for refuting the claim that this disorder pathologizes normative behavior in young children (Keenan et al., 2011). Several studies have shown evidence for the stability of these disorders from preschool to elementary school age. For example, in a study on the predictive validity of ODD in 3- to 5-year-old children, Keenan et al. (2011) showed that 73.0, 66.3, and 51.7% of children diagnosed with ODD at baseline met the criteria at 12-, 24-, and 36-month follow-up, respectively. Similarly, in a Dutch study 62 % of the children who were diagnosed with ODD at the first assessment were diagnosed again at 18-month follow-up (Bunte, Schoemaker, Hessen, van der Heijden, & Matthys, 2014). Significant continuity from age 3 to age 6 for ODD was also shown in the study by Bufferd, Dougherty, Carlson, Rose, and Klein (2012). Likewise, there is evidence for the stability of CD. Keenan et al. (2011) found that of the children who met criteria for CD at baseline, 48.6, 33.3, and 26.0% met criteria at 12-, 24-, and 36-month follow-up, respectively. In the study by Bunte et al. (2014), 35% of the children who were diagnosed with CD at the first assessment were diagnosed again at 18-month follow-up.

Results of these studies support the predictive validity of ODD and CD diagnosis in preschool children, but they also point to instability of diagnosis from preschool to school age. Thus, ODD and CD are disorders that not only show stability but also change in the preschool to early school period. These changes may manifest either in instability of diagnosis (i.e., children with a diagnosis are under remission) or in new cases (i.e., children without a diagnosis at the first assessment are being diagnosed at later assessments). With regard to the latter, in the study by Bunte and colleagues (2014), a substantial number of children without a diagnosis of ODD or CD at the first assessment were diagnosed with one of these disorders at either the 9- or 18-month follow-up. Thus, a preschool child referred for externalizing behavior problems who is not diagnosed with a disorder at the first assessment may show an increase of symptoms and be diagnosed later on, possibly as a result of increasing environmental expectations over the preschool period. Therefore, diagnostic reassessments of preschool children referred for externalizing behavior problems are needed in order to identify new cases and to identify children belonging to the stable ODD and CD groups (Bunte et al., 2014).

In terms of further development of ODD, when two disorders co-occur and do not overlap in time, the term "successive comorbidity" may be used (Angold, Costello, & Erkanli, 1999). It has been shown that ODD and ADHD at age 3 each predict the other disorder at age 6 (Bufferd et al., 2012). Besides this successive homotypic comorbidity, successive heterotypic comorbidity also has been studied. In older children it has been shown that ODD precedes anxiety disorders and depression (Burke, Loeber, Lahey, & Lathouz, 2005; Rowe et al., 2010). However, in preschool children, there was no such successive heterotypic comorbidity between ODD at age 3 and anxiety or

depression at age 6 (Bufferd et al., 2012). On the other hand, successive heterotypic continuity and the relevance of the heterogeneity of ODD symptoms has been investigated by Ezpeleta, Granero, de la Osa, Trepat, and Domenech (2016) from the perspective of irritability. Based on the results of studies on the dimensions of ODD (Rowe et al., 2010; Stringaris & Goodman, 2009a), it has been suggested that the association between ODD and depression or anxiety may be explained by the shared negative affectivity and the irritability component. The study by Ezpeleta and colleagues (2016) traced the developmental course of irritability symptoms in ODD from ages 3 to 5 and examined the psychopathological outcomes of the different trajectories at age 6. Results suggest that for the children in the high-persistence and increasing trajectories of irritability, emotional dysregulation worsened or stayed at a dysfunctional level as they aged. These children's increased difficulties in controlling irritability presented the poorest outcomes in terms of continuity and severity of ODD, internalizing and externalizing comorbidity, functional impairment, and difficulties in anger control. Thus, it seems crucial to identify this subset of children with ODD with a high number of irritability symptoms throughout development in view of preventing comorbid and future adverse longitudinal outcomes.

Regarding the developmental course of ODD, elementary schoolchildren with ODD are at risk for not only CD in early adulthood (Rowe et al., 2010) but also anxiety disorders and depression in adolescence and (early) adulthood (Rowe et al., 2010; Stingaris & Goodman, 2009b). Children with CD are at risk for substance use disorder in early adulthood (Rowe et al., 2010). In addition, a prospective longitudinal study indicated that all adult disorders, including not only antisocial personality disorder and substance use disorder but also anxiety and depressive disorders, were preceded by ODD or CD (Kim-Cohen et al., 2003).

ETIOLOGY

Overview

Many individual and environmental factors that have been identified may play a role in the initiation and persistence of ODD and CD in preschool children. Although we remain far from an integrative theory to explain the development of ODD and CD, we here outline the structure of an overall etiological framework (Matthys & Lochman, 2017). The development of ODD and CD often starts in the toddler years, and maybe even in infancy. Infants and toddlers may show problem behaviors such as restlessness, negativism, and irritability (i.e., temperamental characteristics) that are genetically or environmentally biologically determined (e.g., smoking during pregnancy). In the preschool years, these problem behaviors may develop into symptoms of ODD and CD due to neurobiological factors on the one hand, and the negative parenting behaviors evoked by the child's problem behaviors on the other. Indeed,

coercive parent–child interactions do develop from the preschool years on. These coercive interactions are elicited by the child's maladaptive behaviors, but personality characteristics in the parents, such as impulsivity, contribute to these interactions as well. Moreover, parental behavior and functioning are also affected by contextual factors such as poverty and family discord.

Heritability Estimates

The heritability estimate of antisocial behavior was calculated by Rhee and Waldman (2002) by performing a meta-analysis based on more than 100 twin and adoptive studies. The overall heritability estimate of antisocial behavior was 41%. However, heritability estimates for young children are higher, maybe because the effect of environmental factors, such as peer influence, on antisocial behavior has not yet taken place earlier in childhood. For example, the heritability coefficient for aggression among 3-year-olds is 69% (Van den Oord, Verhulst, & Boomsma, 1996). Similarly, the heritability coefficient for antisocial behaviors that is pervasive across settings among 5-year-olds is 82% (Arsenault et al., 2003).

Importantly, genetic influence is probably stronger for ODD and CD comorbid with ADHD than for ODD and CD only. The heritability estimate for ADHD symptoms is indeed higher than that for antisocial behavior, with percentages ranging from 60 to 88% (Rhee & Waldman, 2002). Most, if not all, of the considerable overlap between hyperactive–impulsive–inattentive and antisocial behaviors can be ascribed to genetic influences they share (Moffitt, 2005). In addition, another characteristic that is relevant to genetic heritability is the presence of callous–unemotional traits. It has been shown that antisocial behavior is more heritable among 7-year-old children with callous–unemotional traits (heritability estimate: 0.81) than in children without these traits (heritability estimate: 0.30) (Viding, Blair, Moffitt, & Plomin, 2005). Thus, when considering the estimate of heritability in preschool and school-age children with ODD and CD, we should take into account the presence or absence of comorbid ADHD and callous–unemotional traits.

TEMPERAMENT

"Temperament" refers to enduring behavioral traits that are comparatively pure in early childhood and become modified with increasing age. From a clinical point of view, temperament is a useful concept to describe behavioral patterns in infants and toddlers who are still too young to diagnose with ODD or ADHD but nonetheless are at risk for the development of these disorders. A number of studies have demonstrated that specific temperamental features precede the occurrence of symptoms of ODD and CD. For example, in the Australian Temperament Project children who at 7 to 8 years displayed both aggressive behavior and hyperactivity had more difficult temperamental

characteristics even at 4–8 months, and increasingly at 32–36 months (i.e., they were more irritable and less cooperative–manageable than normal controls and hyperactive children; Sanson, Smart, Prior, & Oberklaid, 1993). Similarly, maternal ratings of infant fussiness, activity level, predictability, and positive affect during the first year of life, each independently predicted maternal ratings of conduct problems during ages 4–13 years (Lahey et al., 2008).

Neurobiological Domains of Dysfunction

Relevant neurobiological factors are described here from the perspective of three interrelated mental domains: punishment processing, reward processing, and cognitive control (Matthys et al., 2012, 2013). The mental domains in this framework are defined in terms of their functions (e.g., the processing of punishment cues) that are physically realized by the various neurobiological systems (e.g., the amygdala, the autonomic nervous system, and the hypothalamic–pituitary–adrenal [HPA] axis). According to the conceptual framework presented here, adequate functioning of the three mental domains is necessary for adaptive social behavior and development. Children need to be sensitive to punishment cues in order to learn to refrain from inappropriate behaviors. Likewise, normative sensitivity to reward cues is a prerequisite condition for learning appropriate behaviors and for seeking pleasure in natural rewards, such as constructive peer group activities. Finally, in order to behave appropriately, adequate cognitive control of emotions, thought, and behavior is necessary. Some methods, such as structural and functional neuroimaging, used to investigate neurobiological functioning are difficult to apply in young children. However, a number of studies using psychophysiological and neuropsychological methods have been conducted in preschool children.

Punishment Sensitivity

Young children learn to make associations between inappropriate behaviors and (threats of) punishment. Yet children need to be sensitive to punishment cues in order to learn refraining from inappropriate behaviors, which indeed is based on classical (aversive) conditioning. For example, aversive conditioning involves learning to associate hitting another child with subsequent punishment or perception of the distress of the victim. Aversive conditioning is crucial for children, because it results in both anticipatory fear whenever children consider behaving inappropriately and discomfort (e.g., guilt and remorse) occasioned by committed antisocial behavior (Kochanska, 1993). The neurobiological system involved in punishment processing consists of the amygdala, the sympathetic nervous system, and the HPA axis. Studies in elementary schoolchildren and adolescents on amygdala function, cortisol reactivity to stress, and serotonergic and noradrenergic neurotransmission indicate that reduced sensitivity to punishment and aversive cues plays a role in ODD and

CD symptoms (Matthys et al., 2012, 2013). Children and adolescents with ODD and CD may therefore have difficulties in learning to refrain from inappropriate behaviors.

The neural circuit network involved in responsiveness to aversive stimuli also comprises the sympathetic branches of the autonomic nervous system. In a prospective study, fear conditioning using electrodermal responsivity was assessed in children ages 3, 4, 5, 6, and 8. It was shown that poor fear conditioning from ages 3 to 8 years is associated with aggression at age 8 (Gao, Raine, Venables, Dawson, & Mednick, 2010a). Furthermore, it appeared that poor fear conditioning at age 3 predisposes to crime at age 23 (Gao, Raine, Venables, Dawson, & Mednick, 2010b). On a related note, preschool children with a high level of aggressive behavior and those with ODD/CD showed lower basic skin conductance level during video watching (Posthumus, Böcker, Raaijmakers, van Engeland, & Matthys, 2009), which suggests low punishment sensitivity.

Reward Sensitivity

In young children, newly acquired behaviors are likely to become part of their behavioral repertoire when these behaviors are rewarded. Indeed, according to operant conditioning principles, behaviors that are rewarded are more likely to be repeated. In learning new behaviors, classical conditioning is also thought to be involved, that is, in making the association between behaviors and rewarding stimuli. Thus, low sensitivity to reward reduces learning of new appropriate behaviors and learning to substitute inappropriate behaviors with appropriate behaviors, as children typically do (Matthys et al., 2012). In addition, low sensitivity to reward may be associated with unpleasant affect; increased reward seeking, which may manifest in ODD and CD symptoms, then would be an attempt to experience a pleasant level of emotional stimulation (Matthys et al., 2012, 2013). The neurobiological system involved in reward processing consists of the amygdala, the orbitofrontal cortex, and the striatum. Studies in elementary schoolchildren and adolescents on the amygdala, orbitofrontal cortex, and caudate nucleus, and on dopaminergic functioning, indicate that reduced reward sensitivity plays a role in ODD and CD symptoms (Matthys et al., 2012, 2013). Such neuroimaging and neurochemical studies are difficult to conduct in preschool children. However, reward sensitivity may be assessed using a psychophysiological measure.

The preejection period (PEP) of the heart, which is an index of sympathetic nervous system activity, is considered to be a peripheral marker of reward sensitivity (Beauchaine, 2001). PEP nonreactivity to monetary incentives has been shown in male schoolchildren and adolescents with ODD and CD (Beauchaine, Gatzke-Kopp, & Mead, 2007) and in aggressive boys with conduct problems (Beauchaine, Hong, & Marsh, 2008). PEP nonreactivity has also been shown in preschoolers with ODD and ADHD relative to controls (Crowell et al., 2006).

Cognitive Control

In everyday situations, children are continuously faced with problems they need to solve. Various cognitive control or executive functions affect problem solving, such as working memory, set shifting, and inhibition of inappropriate responses (Miyake et al., 2000). These functions are subserved by the frontal cortex. Specifically, the paralimbic system comprising orbitofrontal, superior temporal, cingulate cortices, and limbic brain regions mediates the cognitive control of emotion and motivation (Blair, 2004). Structural deficits and impaired functioning of the paralimbic system have been found in elementary schoolchildren and adolescents with ODD and CD. Likewise, impairments in executive or cognitive control functions, in particular, inhibition and decision making, have been shown in ODD and CD, especially when motivational factors (reward and punishment) are involved (Matthys et al., 2012, 2013). Children and adolescents with ODD and CD are therefore less likely to learn from their mistakes. Consequently, they may not learn to make appropriate decisions in the context of punishment and reward.

According to a meta-analysis, preschool children with externalizing behavior problems perform more poorly on executive function tasks than do typically developing children, with medium effect sizes for overall executive functions and inhibition. Concerning working memory and cognitive flexibility, a small effect size was found (Schoemaker, Mulder, Deković, & Matthys, 2013). In a study with preschool children with ODD/CD impairments in inhibition were found relative to normal controls (Schoemaker et al., 2012). When IQ was controlled, differences were carried mostly by the effect on the task in which motivational demands were high (i.e., when tangible rewards were used). Impaired inhibition in the ODD group comorbid with ADHD was more severe than that in the ODD group. The children were reassessed twice, at 9- and 18-month follow-up. Importantly, the improvement of inhibition performance in children with ODD/CD, with and without ADHD, over time was more pronounced than the improvement of normal controls. ODD/CD children relative to normal controls seemed to catch up a part of their delay (Schoemaker, Bunte, Espy, Deković, & Matthys, 2014).

Parenting Practices and Contextual Family Factors

For over 50 years, research has been conducted on parenting practices in families of children with externalizing behavior problems. Parenting practices that have been found to be linked to children's conduct problems include nonresponsive parenting in infancy, unclear and negative commands, harsh and inconsistent discipline, and lack of warmth and involvement (Reid, Patterson, & Snyder, 2002). It has been shown that deficient parenting practices can interact with children's noncompliance to create coercive cycles of behavior between parents and children that serve as one of the important etiological factors in developing and maintaining children's conduct problems (Reid et

al., 2002). On the basis of numerous studies of meticulous direct observations of child–parent interactions at home, the "coercion mechanism" has been described as a sequence of interactions based on negative reinforcement. The sequence starts with a parent acting aversively toward the child (e.g., giving a negative command, including put-downs). The child may react aversively to this by replying insolently, and the mother gives in. Because the child's reaction "worked," it is more likely to occur again in future exchanges. According to the principle of negative reinforcement, any behavior that terminates an aversive condition is likely to increase in frequency in the future. Thus, preschool children with conduct problems are inadvertently rewarded for their disruptive interactions. There is also evidence that these coercive processes already occur from infancy on and therefore play a role in the emergence of conduct problems; these coercive interactions may be elicited by the child's temperamental characteristics (Patterson, 2002).

A wide array of contextual family factors can affect children's conduct problems, ranging from poverty to family discord and parent psychopathology. Low socioeconomic status, assessed as early as preschool, has predicted teacher- and peer-rated behavior problems at school (Dodge, Pettit, & Bates, 1994). Rather than having a simple, direct effect on children's behavior, poverty affects other family processes, especially parenting practices, which then mediate the effect of poverty (Maughan, 2001). Similarly, there is an increasing risk for coercive processes to occur in the presence of family discord and parent psychopathology (Cappaldi, DeGarmo, Patterson, & Forgatch, 2002). Indeed, in order to give positive commands, to be consistent, to ignore mild misbehaviors, and to use mild punishment after serious misbehaviors, a number of preconditions need to be fulfilled, such as having a positive attitude, feeling inner peace, and supporting each other. These preconditions are not fulfilled in case of parental depression or ADHD, and marital discord (Shaw, Hyde, & Brennan, 2012).

CLINICAL ASSESSMENT

In the clinical assessment, the collected data are needed by the clinician in order to make decisions with respect to diagnosing a child according to DSM-5, to generate hypotheses about etiology, and to propose a treatment plan to the parents and children. With respect to categorical diagnosis, there is a risk of idiosyncratic decision making if the clinician only uses so-called "open" or clinical interviews, because the clinician may focus on a particular set of symptoms and fail to explore the full range of psychopathology. The unreliability of clinical methods has led to the development of standardized rating scales and structured interviews. In addition, structured observation methods have been developed. In everyday clinical practice, the decision to diagnose a child with ODD or CD is not based on the results of a single measure but on the combination of results from multiple measures, such as standardized

parent and teacher/caregiver rating scales; a (semi)structured, DSM-oriented interview; and structured observation (Matthys & Lochman, 2017).

Rating Scales

It is appropriate to use one of the comprehensive standardized rating scales that assess a number of areas of adjustment rather than a single domain of behavior. Moreover, because they have been standardized using large normative samples, the referred child's ratings on a given scale can be compared with those of typically developing children. Thus, scores give a quick view of whether the child functions within the clinical or normal range of various domains (Matthys & Lochman, 2017).

The Achenbach System of Empirically Based Assessment (ASEBA; Achenbach & Rescorla, 2000) family of instruments is widely used and has been standardized in many countries. For children ages 1.5–5 years, there is a 100-item version to be completed by parents (Child Behavior Checklist; CBCL/1.5–5) and caregivers/teachers (Caregiver/Teacher Report Form; C-TRF/1.5–5). The ASEBA instruments yield Total, Internalizing and Externalizing broad-band and narrow-band scales. The CBCL/1.5-5 Externalizing broad-band scale comprises the narrow-band scales Aggressive Behavior and Attention Problems. On the other hand, the CBCL/6–18 Externalizing scale comprises Aggressive Behavior and Rule-Breaking Behavior (Achenbach & Rescorla, 2001). Thus, Attention Problems is not part of the Externalizing scale in the CBCL/6–18, whereas it is in the CBCL/1.5–5. This also holds true for the Caregiver/Teacher versions.

A much briefer comprehensive scale is the Strengths and Difficulties Questionnaire (SDQ; Goodman, 1997). The SDQ has been studied less extensively than ASEBA, but the number of studies in various countries is increasing (see special issue of *European Child and Adolescent Psychiatry, 13,* Suppl. 2, 2004). The SDQ consists of 25 items. Among the many forms, those for parents and teachers of 3- and 4-year-olds and of 4- to 10-year-olds are relevant here. These forms can be downloaded free of charge from *www.sdqinfo.com*. The SDQ asks about 25 attributes. It yields five scales: Hyperactivity, Emotional Symptoms, Conduct Problems, Peer Problems, and Prosocial. Norms for the United Kingdom, the United States, Australia, Finland, Sweden, and Germany can be found on the website.

The Behavior Assessment System for Children–Second Edition (BASC-2; Reynolds & Kamphaus, 2004) assesses a wide range of adjustment difficulties in children and adolescents ages 2–21. The BASC has forms for parent, teacher and child (ages 8–21). It has been standardized for the United States. Besides two conduct problem domains (Aggression and Conduct Problems), many other domains are assessed as well: Adaptability, Anxiety, Attention Problems, Atypicality, Depression, Hyperactivity, Leadership, Learning Problems, Functional Communication, Social Skills, Somatization, Study Skills, Withdrawal, Activities of Daily Living, Attitude to School, Attitude

to Teachers, Interpersonal Relations, Locus of Control, Relations with Parents, Self-Esteem, Self-Reliance, Sensation Seeking, Sense of Inadequacy, and Social Stress.

In contrast to the previously mentioned comprehensive rating scales, a number of specific questionnaires have been developed. First, the Conners' Rating Scales—Revised (CRS-R; Conners, 1997) have a primary emphasis on externalizing problems. The CRS-R has forms for parent (CPRS-R), teacher (CTRS-R), and adolescent (CASS). Each measure has a short version (including Oppositional and Hyperactivity scales) and a long version. The parent and teacher versions are intended for use with children ages 3–17 years. Second, the Multidimensional Assessment Profile of Disruptive Behavior (MAP-DB) is a questionnaire measure that specifically assesses four dimensions of disruptive behavior: Temper Loss, Aggression, Noncompliance, and Low Concern for Others (Low Concern comprises two subdimensions: Disregard for Others and Punishment Insensitivity) theorized to be defining features of disruptive behavior syndromes (Nichols et al., 2015; Wakschlag et al., 2014). Finally, the Inventory of Callous–Unemotional Traits (ICU; Frick, 2004), developed for older children, may also be used in preschool children (Ezpeleta et al., 2013). The ICU includes 24 items coded on a 4-point scale and covers three dimensions: Callousness (11 items), Uncaring (eight items), and Unemotional (five items).

Structured Diagnostic Interviews

A number of structured and semistructured parent-report diagnostic interviews have been developed for use with young children; often these have been adapted from interviews with older children. They include interviews such as the Diagnostic Interview of Children and Adolescents for Parents of Preschool and Young Children (DICA-PPYC; Ezpeleta, de la Osa, Granero, Domenech, & Reich, 2011), the Kiddie Disruptive Behavior Disorders Schedule (K-DBDS; Keenan et al., 2007), the Preschool Age Psychiatric Assessment (PAPA; Egger, Ascher, & Angold, 1999), and the Schedule for Affective Disorders and Schizophrenia for School-Age Children—Present and Lifetime versions (K-SADS-PL) for the assessment of preschool children (Birmaher et al., 2009).

The reliability and validity of these interviews for preschool children have been studied intensively. For example, the K-DBDS has been shown to have satisfactory interrater and test–retest reliability with regard to ODD and CD symptoms in the United States and in the Netherlands (Bunte, Schoemaker, Hessen, van der Heijden, & Matthys, 2013; Keenan et al., 2007). In addition, the predictive validity of ODD and CD diagnosis has been demonstrated (Bunte, Schoemaker, et al., 2013; Keenan et al., 2011). Clinical usefulness was demonstrated by studying validity on an individual level (Bunte, Schoemaker, et al., 2013). With a sensitivity of 87% and a specificity of 93% for ODD (Bunte, Schoemaker, et al., 2013) it is important to keep in mind that

diagnosing a child with ODD is based on information from not only the parent but also the teacher/caregiver, and from clinical observation.

Observational Methods

Although parent reports are based on children's behaviors on a daily basis, these reports may be biased due to a number of factors, such as personality characteristics of the parents (Collishaw, Goodman, Ford, Rabe-Hesketh, & Pickels, 2009). Therefore, direct observation that is not filtered through the perceptions of the parent may provide a different window on the child's functioning (Le Couteur & Gardner, 2008). Clearly, a limitation of observation is its brevity and contextual dependency; in other words, the behaviors observed need not be representative of all problem behaviors (Le Couteur & Gardner, 2008). Even though clinicians do not expect to observe each symptom, they may want to see at least "the tip of the iceberg." Thus, although generation of the presumption of the presence of ODD or CD may be based on information from parents and teachers, direct observation may be used to support this presumption or not. In addition, clinical experience suggests that many parents desire the clinician to observe the child in order to arrive at a diagnosis, because parents who consult a clinician have difficulty accepting that the decision about the presence or absence of a disorder would be based only on parent and teacher reports; parents want clinicians, themselves, to "look at their child" (Bunte, Laschen, et al., 2013).

Various observational tools have been developed, such as the Dyadic Parent–Child Interaction Coding System (DPICS; Robinson & Eyberg, 1981), a short (15 minutes) observational assessment of parent–child interaction that is sensitive to treatment change. Therefore, it has often been used to evaluate behavioral parent training for young children with conduct problems (e.g., Posthumus, Raaijmakers, Maassen, van Engeland, & Matthys, 2012).

Wakschlag, Briggs-Gowan, et al. (2008; Wakschlag, Hill, et al., 2008) developed the more extended (60 minutes) Disruptive Behavior Diagnostic Observation Schedule (DB-DOS), a highly structured method that allows the child's behavior to unfold during a variety of challenging and pleasurable activities or tasks. These tasks, lasting approximately 5 minutes, tap into compliance, frustration, social interaction, and internalization of rules. The DB-DOS is composed of three interactional modules or contexts: one parent–child module and two examiner modules. In the first examiner module, the examiner is normally responsive to child behavior. This is the examiner active support module. Then, within the context of minimal support, the child is observed while working independently, with the examiner being busy doing his or her own work (Wakschlag & Danis, 2004). Examiner-based assessments are designed to be clinically sensitive by standardizing adult responses in a manner that presses for a range of clinically salient behaviors in the child; however, they lack the ecological validity of parent–child assessments. Therefore, combining examiner- and parent-based behavioral observation

paradigms provides complementary methods for incorporating the interactive nature of social behavior into the assessment of clinical significance (Wakschlag, Hill, et al., 2008).

Reliability (internal consistency, interrater reliability, test–retest reliability) and validity (convergent and divergent) of ODD and CD have been demonstrated in clinical samples in the United States and in the Netherlands (Wakschlag, Briggs-Gowan, et al., 2008; Wakschlag, Hill, et al., 2008; Bunte, Laschen, et al., 2013). In addition, clinical usefulness was demonstrated by studying validity on an individual level. It was shown that the DB-DOS Behavioral Regulation score supported approximately 60% the ODD or CD diagnosis generated by the information from parents, teachers (caregivers) and cognitive assessment using the best-estimate diagnosis. Thus, for six out of 10 children diagnosed with ODD or CD, this diagnosis has been confirmed (or not) by the DB-DOS (Bunte, Laschen, et al., 2013).

TREATMENT

Parent Training

Parent training is a psychotherapeutic method in which parents either individually or in a group are trained to change the behavior of their children using social learning techniques. These techniques are based on operant conditioning, the learning theory according to which behavior develops and can be altered by focusing on its antecedents and on its consequences (Kazdin, 2005). In addition, observational learning also is crucial. According to this learning theory, one learns by observing another individual (a model) engage in behavior without performing the behavior him- or herself (Bandura, 1973). Thus, parents learn appropriate parenting skills by observing other parents, the therapist, or models from videotapes.

The goal of parent training is to change the child's referral problems by improving the parents' skills that affect parent–child interactions. Typically, programs consist of a series of sessions, each of which covers a specific operant conditioning principle and related procedures. Thus, programs include sessions on positive reinforcement and the use of praise and tokens, sessions focusing on extinction and ignoring, mild punishment and the use of time-out, and response cost and loss of privileges. Because practicing the parenting skills at home is essential in parent training, sessions begin by reviewing the parents' experiences with the skills covered the previous week. Then, a new principle and related procedures are presented. The skills are practiced using role play (i.e., with other parents or with the therapist playing the role of the child) and *in vivo* practice (i.e., with the child), with the therapist providing support, feedback, and modeling. Finally, assignments to practice the skills at home are discussed. Between sessions the therapist is available to the parent to address problems in implementing the skills at home. Moreover,

when training is delivered in a group format, parents may support each other between sessions.

Two programs have been developed specifically for young children: the Incredible Years (IY; Webster-Stratton, 2001) and parent–child interaction therapy (PCIT; Brinkmeyer & Eyberg, 2003). IY is delivered in a group format and includes the use of videotapes and a book on parenting skills (Webster-Stratton, 2005). A collaborative relationship between therapist and parents is developed. The use of a book enables parents to prepare for sessions by reading a chapter on the skills that are the topic of the session, avoiding a didactic approach that may result in resistance in parents. Videotapes of real-life parent–child, child–child, and parent–parent interactions elicit group discussions on specific problem behaviors and how to handle them. Following videotapes, therapists ask open questions to elicit discussions and problem solving by parents. Therapists therefore avoid giving direct answers and advice as experts. Instead, a collaborative relationship is established in which the therapist's and the parents' knowledge, strengths, and perspectives are utilized equally. The group format enables parents to support each other during the sessions and to serve as "buddies," helping each other complete home assignments between sessions.

In each of the 18 sessions (2 hours per session), eight to 12 parents participate. The program starts with "how to play with your child." Parents learn to follow the child's lead, to pace at the child's level, to praise and encourage the child's ideas and creativity, and to use descriptive comments instead of asking questions. The program then focuses on the appropriate use of praise. In addition to the basic skills of praising children, parents learn to praise their child in front of other people (e.g., the mother praises the child in the father's presence), to praise themselves, and to model self-praise. With regard to a token economy, it is stressed that parents of young children make the program simple and fun, avoid mixing rewards and punishment, and gradually replace tokens with social approval. In the sessions on limit setting, parents learn to make commands short, positive and polite. Thus, "stop" and "don't" commands ("Don't shout") should be avoided and replaced by "do commands" ("Speak softly"). Finally, skills to handle inappropriate behaviors are taught. In these sessions, parents learn to consistently ignore mildly inappropriate behaviors by moving away from the child, avoiding eye contact and discussion, then returning attention to the child as soon as misbehavior stops. Parents also learn to use time-out appropriately. They learn to explain the time-out procedure to the child, to practice time-out with the child, to be polite and calm when sending the child to time-out, to ignore the child while in time-out, to use loss of privileges for not going to time-out, and to give the child the opportunity to behave appropriately after time-out. Evidence for the effectiveness of IY has been examined in a meta-analytic review including 50 studies (Menting et al., 2013). Treatment studies using parent report were associated with larger effect ($d = 0.50$) than indicated ($d = 0.20$) and selective

(d = 0.13) prevention studies. Initial severity of child behavior was the strongest predictor of effects.

PCIT is given on an individual basis. In comparison with other programs, two essential characteristics of PCIT are the participation of both the child and the parent in all sessions and coaching by the therapist while the parent is playing with the child. If a one-way mirror is available, the coaching is done using a "bug in the ear"; if not, the therapist coaches the parent in a low voice while next to the parent. Thus, the therapist shapes the parent's behavior using prompts, reinforcement, and corrective statements. Families meet for weekly, 1-hour sessions for an average of 12–16 sessions. PCIT has two segments: child-directed interaction and parent-directed interaction. In child-directed interaction, the therapist teaches parents the skills to foster attachment and relations, such as praising the child's behavior, reflecting the child' statements, imitating the child's play, describing the child's play, and using enthusiasm. In parent-directed interaction, parenting skills such as giving clear instructions and giving time-out are taught. PCIT is highly individualized. At the beginning of the session, parent–child interaction is observed in order to decide which skills to work on during the session. In line with this, there is no limit in the number of sessions. Instead, treatment is performance based and continues until parents express confidence (and demonstrate the skill) in their ability to manage child behavior. Numerous studies that have examined the effectiveness of PCIT as a treatment are included in a meta-analysis (Thomas & Zimmer-Gembeck, 2007). When compared to wait list, medium effects, similar to IY treatment studies, were found to favor PCIT for parent reports of child's negative behavior. See Elkins, Mian, Comer, and Pincus (Chapter 11, this volume) for a detailed account of PCIT and its adaptations.

Child Training

Child training programs have been developed as part of multicomponent interventions. For example, Dinosaur School addresses issues that young children with conduct problems frequently face: social skills problems; inability to empathize emotionally or engage in perspective taking; effective conflict resolution; and dealing with feelings of loneliness, stress, and anger (Webster-Stratton & Hammond, 1997). IY Dinosaur School—Child Training was initially developed as part of a larger preventive intervention designed to examine the relative and additive effectiveness of parent training and child training for 4- to 7-year-olds with early-onset conduct problems. Analysis of treatment groups revealed that the child training led to a significant reduction in the amount of conduct problems reported in the home and increases in social problem-solving skills in comparison to controls. One-year follow-up assessments indicated that these changes had been maintained over time. In addition, the combination of child and parent training proved superior to each

of the component pieces in terms of the clinical significance of the results at 1-year follow-up (Webster-Stratton & Hammond, 1997). There is, however, insufficient evidence for the effect of child training to use it in clinical practice without additional training of parents or teachers.

Classroom Intervention

The IY training series also includes the Teacher Classroom Management Training component (Webster-Stratton, 2005). The teacher curriculum was created to strengthen teachers' classroom management skills, to foster their use of effective discipline strategies and reinforce prosocial child behaviors, and to increase teachers' ability to teach and reinforce social–emotional skills in the classroom. The curriculum also includes strategies for strengthening home–school connections. The effectiveness of the combined parent and teacher curriculum in the context of Head Start has been studied. Evaluations demonstrated improvements in children's behavior in the classroom and in teachers' management skills. In particular, teachers in experimental classrooms showed better classroom management, including more positive and less harsh and critical techniques, than control teachers (Webster-Stratton, Reid, & Hammond, 2001).

Psychopharmacological Treatment

According to American Academy of Child and Adolescent Psychiatry guidelines for psychopharmacological treatment in young children, psychosocial interventions constitute first-line treatment of ODD and CD (Gleason et al., 2007). These interventions have been shown to be effective in young children with disruptive behavior problems (Comer, Chow, Chan, Cooper-Vince, & Wilson, 2013). Unfortunately, the proportion of young children actually receiving psychotherapy has decreased significantly in the United States in recent years, whereas use of antipsychotic medications has increased (Comer et al., 2013).

Although, according to American and Dutch guidelines, psychopharmacological treatment is not indicated in mild forms of ODD or CD, with or without ADHD, starting a trial with psychostimulants is indicated in severe forms of ODD or CD comorbid with ADHD and not responding to psychotherapy (Gleason et al., 2007; Matthys & van de Glind, 2013). Methylphenidate is the first-choice medication. The efficacy of methylphenidate in preschoolers with ADHD has been demonstrated in the Preschool ADHD Treatment Study (PATS; Greenhill et al., 2006), in which half of the children had ADHD comorbid with ODD. Aggressive/defiant symptoms were affected as strongly as symptoms of ADHD (Greenhill et al., 2006). The presence of comorbid disorder(s) on the efficacy of methylphenidate was investigated by Ghuman and colleagues (2007). In preschoolers with ADHD, the presence of no or one

comorbid disorder (primarily ODD) predicted a large treatment response at the same level as has been found in school-age children. Preschoolers with two comorbid disorders had moderate treatment response, and preschoolers with three or more comorbid disorders did not respond to methylphenidate (Ghuman et al., 2007). See Tandon (Chapter 5, this volume) for further details on ADHD diagnosis and treatments.

Methylphenidate has adverse effects such as difficulty falling asleep, a decrease in appetite, and an increase in irritability; the latter often is temporary. There are probably more adverse effects in preschoolers than in school-age children (Wigal et al., 2006). Since the mean optimal dose for preschoolers is slightly lower than that for school-age children (Greenhill et al., 2006), starting at lower methylphenidate doses may improve tolerability in preschoolers (Greenhill, Posner, Vaughan, & Kratochvil, 2008).

Recommendations regarding pharmacotherapy for preschool children with ODD or CD and severe aggression without ADHD differ among countries. The U.S. Preschool Psychopharmacological Working Group recommended risperidone as one effective medication once psychotherapies have failed. Canadian and Dutch guidelines are more reluctant to prescribe risperidone in children due to side effects such as weight increase and possible endocrine effects (Gorman et al., 2015; Matthys & van de Glind, 2013). Although a number of studies have shown the efficacy of risperidone for the treatment of aggressive behavior in children and adolescents (for a recent overview of pharmacological studies in ODD and CD, see Pringsheim, Hirsch, Gardner, & Gorman, 2015a, 2015b), to our knowledge no such studies in preschool children have been conducted. As an alternative to risperidone, a trial with psychostimulants is recommended (Matthys & van de Glind, 2013), because there is some evidence of an effect of psychostimulants on aggression, independent of the effect on ADHD symptoms in schoolchildren and adolescents with CD (Klein et al., 1997). When methylphenidate is not effective, a trial with risperidone is recommended (Matthys & van de Glind, 2013).

CONCLUSIONS

ODD and CD are valid disorders that can be reliably diagnosed in preschool children. These disorders show stability, as well as change, in the preschool to early school period. Diagnostic reassessments of preschool children referred for externalizing behavior problems are therefore needed in order to identify children belonging to the stable group of ODD and CD, and to identify new cases among preschool children referred for externalizing behavior problems not previously diagnosed as ODD or CD at an initial assessment. Monitoring of the child's development in terms of symptoms and associated impairment is needed in view of possible adaptation of treatment. This is important, because effective intervention methods are available and may prevent future, adverse longitudinal outcomes.

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5

Attention-Deficit/Hyperactivity Disorder in Preschoolers

Background, Assessment, and Treatment

Mini Tandon

Attention-deficit/hyperactivity disorder (ADHD) has been described as a developmental or maturational delay in response inhibition (Barkley, 1997), delay aversion (Sonuga-Barke, 2003), and, in addition, encompasses certain temperamental characteristics (Nigg, Goldsmith, & Sachek, 2004). Empirical findings in support of the validity of ADHD as a disorder in preschool-age children has grown in recent years and since the first edition of this book (e.g., Chacko, Wakschlag, Hill, Danis, & Espy, 2009; Luby, 2006). Support of the validity of the diagnosis of ADHD in preschool-age children has been demonstrated in examination of executive function deficits often characteristic of older age children with ADHD (Schoemaker et al., 2012; Tandon, Belden, & Luby, 2009; Wiebe, Espy, & Charak, 2008; Wiebe et al., 2011). Executive functions are thought to develop in a nonlinear manner for the first 5 years of life, and this may be why capturing these deficits is not without challenges (Garon, Bryson, & Smith, 2008; Rothbart & Posner, 2001). The association of neuropsychological deficits with concurrent or later ADHD symptoms has been investigated (Pauli-Pott & Becker, 2011). Findings included larger effect sizes and magnitudes for response inhibition and delay aversion than for working memory. Several functions decreased in effect size by increasing age, such as delay aversion, while interference control tasks and continuous performance tests seem to increase in effect size by increasing age, suggesting critical time periods for assessment of such neuropsychological domains to be useful correlates to ADHD symptoms (Pauli-Pott & Becker, 2011). Further

validation of ADHD in preschoolers has been demonstrated in neuroimaging studies. Dopamine pathways involving at least prefrontal, cingulate, and striatal regions are thought to be implicated in ADHD, and undergo dynamic changes from birth through age 5 (Garon et al., 2008). Though still in its early stages, neuroimaging that involves preschool-age children with ADHD suggests that severity of hyperactive–impulsive symptoms are correlated to basal ganglia but not to cortical volumes, as in school-age children (Mahone et al., 2011).

EPIDEMIOLOGY

Prevalence estimates of ADHD in preschool-age children approximate that in school-age children, ranging from 2 to 8% (Egger & Angold, 2006). As noted in school-age children, preschool-age children with ADHD exhibit problems in domains of socialization, school performance, and overall behaviors (DuPaul, McGoey, Eckert, & VanBrakle, 2001). The diagnosis has been demonstrated as stable within the preschool years, with the latter years showing more stability than diagnoses made between ages 3 and 4 (Tandon, Si, & Luby, 2011). Stability of diagnosis but not subtypes into school age has also been demonstrated in a number of samples, both clinical and community samples (Lavigne et al., 1998; Lahey et al., 2004; Lahey, Pelham, Loney, & Willcutt, 2005). Comorbidity with preschool ADHD is common (Wichstrom et al., 2012) and occurs in clinical samples most often with disruptive disorders (64%), including oppositional defiant disorder (ODD; 62%) and conduct disorder (CD; 23%), and internalizing disorders such as depression (42%) and anxiety (28%) (Wilens et al., 2002). Preschool boys are almost twice as likely as girls to be diagnosed as ADHD (Egger & Angold, 2006).

ASSESSMENT

Similar to the comprehensive assessment of the preschool-age child for any disorder, the evaluation for ADHD ideally occurs over several time points, with several informants and caregivers, and utilizes objective measures. Clinicians' serial observations in the clinic, home, and/or day care/school settings can be essential to the accuracy of diagnosis (Luby & Tandon, 2010; O'Neill, Schneirderman, Rajendran, Marks, & Halperin, 2014; Wakschlag et al., 2005). The multiple tools that are available for the assessment of ADHD in preschoolers are often utilized more in research than in clinical settings. These areas of assessment have been summarized to include behavioral rating scales, measures of attention and hyperactivity/impulsivity, structured interviews, and observations (Smith & Corkum, 2007). The empirical literature supports weak-to-medium associations between rating scales and laboratory measures of ADHD (Barkley, 1991, 2006; Conners, 2004; O'Neill et al., 2014). One

of the most utilized of these scales has been the Conners parent and teacher rating scales (Conners, 2001) validated in children as young as age 3. The Child Behavior Checklist (CBCL/1.5–5; Achenbach & Edelbrock, 1991) can be a helpful tool to assist in recognition of elevations in the attention domain, while assessing for comorbid symptomatology and adding adaptive functioning. Both the Conners scales and CBCL have demonstrated good criterion validity and interrater reliability (Sattler & Hoge, 2006).

As in school-age children, a combination of clinician, teacher, and parent report is used in concert to determine impairment in two settings. Low agreement among these informants is the rule rather than the exception (O'Neill et al., 2014). The prognostic value of specific informants' ratings of younger preschoolers to predict ADHD at 6 years of age varies, with some evidence suggesting that parent and clinician are more predictive than teacher report at this age (O'Neill et al., 2014). Nonetheless, a combination of all informants is still obtained when feasible to establish cross-situationality, critical to the diagnosis (Dirks, De Los Reyes, Briggs-Gowan, Cella, & Wakschlag, 2012; O'Neill et al., 2014). The Caregiver–Teacher Report Form (for children ages 1.5–5 years; Achenbach & Rescorla, 2000) may be used in children not enrolled in preschools but in other routine caregiving environments common to this age. A number of continuous performance tests exist and are used to elucidate specific areas of executive function that can be problematic in ADHD, but the use of these measures is not characteristic of everyday clinical practice with preschool children (Mahone, Pillon, Hoffman, Hiemenz, & Denckla, 2005). The test may be hard to execute, with infrequent response demands for 3- to 4-year-olds, and may be experienced as lengthy. Errors of omission and commission may help delineate problems with inattention, impulsivity, and reaction time variability. Though less utilized in preschoolers, some studies suggest that commission errors at age 4.5 years significantly predict ADHD symptoms in third grade (Von Stauffenberg & Campbell, 2007); however, in general, the use and validity of CPTs are not clearly established in clinical or research practice with preschoolers (Barkley, 1991; Preston, Fennell, & Bussing, 2005). As a group, neuropsychological tests in preschoolers show good concurrent validity, distinguishing preschoolers with ADHD from their non-ADHD peers but they appear to have poor prognostic value for later diagnosis of ADHD in the school years (Rajendran, O'Neill, Marks, & Halperin, 2015).

TREATMENT

As in other psychiatric disorders impacting preschool-age children, psychotherapy is the first line of treatment for ADHD (Gleason et al., 2007; Tandon & Luby, 2009). However, when therapy resources are not available, and severity of symptomology and impairment is high, medications for ADHD are often used (Garfield et al., 2015).

Nonpharmacological Treatment

Because ADHD often co-occurs with disruptive and internalizing disorders, empirically based therapies that originated for disruption and/or for enhancement of relational and parenting skills have often been used (Sanders, Markie-Dadds, & Turner, 2000; Wagner & McNeil, 2008; Webster Stratton & Hancock, 1998). Behavioral parent training (BPT) has been well described by Barkley (2006) and can be implemented in preschoolers (Chronis, Chacko, Fabiano, Wymbs, & Pelham, 2004). On average, eight to 12 weekly sessions lasting 60 to 90 minutes are reported, depending on individual or group formats, respectively (Barkley, 2006; Cunningham, Bremner, & Secord-Gilbert, 1998). Key components to parent training include selective attention to positive behaviors, education on ADHD itself, and setting effective commands and time-outs, along with optimizing environmental strategies. Education on effective monitoring in schools is also incorporated (Barkley, 2006; Chronis et al., 2004). Of key importance is that improvements in ADHD symptoms per se are less evident than those seen for family conflict, disruptive behaviors, and parenting stress associated with ADHD (for review, see Barkley, 2006, 2015).

Another empirically based psychotherapy format used in groups of parents of preschoolers with ADHD is Community Parent Education (COPE; Cunningham et al., 1998), which utilizes a group format to disseminate behavioral parenting therapy and make it widely available in community settings such as schools. COPE modules were used prior to methylphenidate trials in the Preschool ADHD Treatment Study (PATS) described below. Aside from behavioral parent training and parent–child dyadic therapies, there is limited to no evidence that directly teaching the preschool-age child to self-regulate will improve ADHD symptomatology or impairment, despite its appeal at face value (Rajwan, Chacko, & Moeller, 2012). Limited data exist to support that nonpharmacological treatments generalize across symptom domains or contexts (e.g., treating inattention will not necessarily improve peer relations, and treating impulsivity as it occurs at home may not result in improvement in the schools). Therapist skill and adherence to protocol fidelity, along with parental engagement, are essential to optimize results (Sonuga-Barke, Thompson, Daley, & Laver-Bradbury, 2004; Barkley, 2006). Multimodal interventions, in which several individuals (including parents, teachers, and child), and settings are comprehensively targeted have shown promise in reduction of teacher and parent-reported behaviors and preacademic skills (Barkley et al., 2000; Kern et al., 2007; McGoey, DuPaul, Eckert, Volpe, & Van Brackle, 2005; Rajwan et al., 2012). Parental engagement rates as low as 25–35% were reported as one possible reason for inconsistent improvements in parent-rated outcomes (Williford & Shelton, 2008). Combined programs, in which BPT is combined with a child therapy (e.g., child-specific socioemotional and behavioral trainings like the combined Incredible Years curriculum; Webster-Stratton, Reid, & Beauchaine, 2011) report BPT parent engagement rates at 80%,

and a resulting 75% of parents reporting improved outcomes (for review, see Rajwan et al., 2012).

Psychosocial Support

Development of an individualized education plan (IEP) as early as possible for young children with ADHD is highly encouraged and often is available in public school districts with early childhood programming. A school diagnosis is often referred to as "other health impaired" and may include accommodations such as a child sitting in front of the class, taking scheduled breaks, and/or being allowed extended time for tests. During comprehensive school and neuropsychological testing, comorbid reading disorder (19%; Carroll, Maughan, Goodman, & Meltzer, 2005) and learning disability (44%; Pastor & Reuben, 2008) that may co-occur with ADHD should be addressed as part of the comprehensive treatment plan. Despite goals to improve ADHD symptomatology, addressing functional impairments may be the most important focus to change poor developmental trajectories associated with ADHD (Pelham & Fabiano, 2008). Specifically, severity of ADHD symptoms may account for only 10% of the variance in impairment by some estimates (Gordon et al., 2006). Furthermore, despite early childhood interventions, prognosis may be poor, and it has been recommended that ADHD be treated as a chronic condition, regardless of age of onset (American Academy of Pediatrics, 2011).

Pharmacological Treatment

ADHD is one of the disorders in the preschool period for which medication is most often prescribed (Visser et al., 2014). Stimulants remain the mainstay of treatment after nonpharmacological interventions have failed to improve symptoms in preschoolers with ADHD. Most of the empirical data informing use of stimulants in preschoolers has been specific to methylphenidate and investigated in a multisite, randomized, placebo-controlled study, the PATS, the largest multisite treatment study for ADHD in preschoolers (Greenhill et al., 2006; Kollins et al., 2006). A number of manuscripts have been published on the design, safety, side effects, pharmacogenetics, and outcomes, both short and long-term (Abikoff et al., 2007; Swanson et al., 2006; Vitiello et al., 2007; Wigal et al., 2006). Despite the challenges, the study findings have further served to inform about the nature of side effects, such as increased irritability and less efficacy compared to use in school-age children (Greenhill et al., 2006; Wigal et al., 2006). Furthermore, a conservative approach was used, first with psychotherapy first for 10 weeks from COPE modules, and only those children who did not improve by 30% on the Conners rating scales after the therapy were then eligible to enroll in the next phase of pharmacological treatment (Greenhill et al., 2006). The study also informed a wide range of optimal doses of methylphenidate, though the average dose was 20 mg/day in divided doses (Greenhill et al., 2006).

The most recent data indicate that at 6-year follow-up of children treated

in this study, severity and symptoms in children with moderate to severe ADHD persist despite medication (Riddle et al., 2013). See Gleason and Teverbaugh (Chapter 15, this volume) for additional details.

Other Treatments

Other treatments have been described but with mixed evidence, including dietary recommendations such as restriction diets, which may have some benefits to about 30% of children with ADHD (Nigg, Lewis, Edinger, & Falk, 2012). Artificial food coloring has also been investigated to determine its role in ADHD. Some effects were found in randomized controlled trials, but based on recent meta-analyses, additional investigation is warranted because current studies have been derived from smaller sample sizes and with potential publication bias (Nigg et al., 2012). In addition to potential publication bias, many recent studies that have found effects of food color on ADHD have been qualitative and have not specified magnitudes of effect. Some studies also used food colors that are not currently approved for use by the U.S. Food and Drug Administration (FDA; Nigg et al., 2012; Jacobson, 2008; Stevens, Kuczek, Burgess, Hurt, & Arnold, 2011). Conversely, the European Union Parliament has now required warning labels on specific food colors based on a community-based study in which food colors contributed to hyperactivity symptoms (McCann et al., 2007). Sugar and artificial sweeteners have been examined in at least five randomized controlled trials with no detectable change in ADHD symptoms; however, these studies used small sample sizes over short periods of time (Heilskov Rytter et al., 2015). Taken together, there continue to be mixed findings for dietary contributors, and at this time, there is no mechanism to determine which individual children with ADHD are affected by such contributors (Nigg et al., 2012). Neurofeedback and other behavioral therapies may also have limited effects on symptoms of ADHD when blinded studies are evaluated. Further studies are needed that are specific to preschool-age children before implementing treatment recommendations for ADHD (Sonuga-Barke et al., 2013).

CONCLUSIONS

In summary, opinion in the field has moved from whether ADHD exists in preschool-age children to how to accurately diagnose and optimize treatment and functional outcomes. A number of risk factors that may contribute to development of ADHD are not limited to low birthweight, *in utero* exposures, and sensitivities to dietary factors; heritability continues to be the largest contributor. Psychotherapy remains the mainstay in preschool ADHD, and parent training has the most empirical evidence at this time; however, a number of additional therapies that target functional deficits such as social skills, and IEP development at the school level may ultimately have the largest impact on functional outcomes. Psychopharmacological interventions treat symptoms

and not underlying deficits. They are used when therapies fail or when severity of symptoms warrants more intensive treatment of preschool-age children. However, preschoolers are more sensitive to the side effects of stimulants, and efficacy rates are lower than those in school-age children. Comprehensive and early diagnosis and treatment are warranted, because longitudinal stability of ADHD into school age is established, along with a host of poor psychosocial outcomes and risks. Recent advances in imaging may help to inform neurocircuitry of this complex and heterogeneous disorder, but dopamine pathways continue to be most implicated.

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6

Anxiety Disorders

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Anxiety disorders are the most common class of psychiatric illnesses in any age group, including preschoolers. This chapter provides a selective review of topics related to preschool anxiety disorders, including normative versus atypical fear, classification, assessment, epidemiology, long-term impact, and neurobiology. Treatment is reviewed here briefly and covered in more detail in Part III of this handbook. While the studies reviewed provide an emerging picture of preschool anxiety disorders, we highlight many areas in which more work is needed to elucidate these common conditions.

NORMATIVE FEAR VERSUS ANXIETY DISORDERS

The terms "fear" and "anxiety" refer to related but differentiable phenomena. Fear is an immediate and rapidly evolving emotional response to real or perceived imminent threats in the environment. Anxiety is a more sustained, heightened state of apprehension in anticipation of future threats. Both fear and anxiety are normal human emotions associated with a range of physiological and behavioral manifestations that are typically adaptive responses to threat. Components of both fear and anxiety may include increased physiological arousal, such as elevated heart rate, increased alertness, increased motor reactivity, and potentially a fight-or-flight response. Fearful facial expressions and more overt signs of fear, such crying in a young child, serve as an important means of communication, signaling to caregivers that the child is under threat and promoting protective behaviors from the caregiver. Given its adaptive utility, it is not surprising that fear follows a well-defined developmental

trajectory in which infants tend to exhibit fear in specific situations at specific ages. Although some fear behaviors are exhibited in very early infancy, reliable fear is detected around age 9 months, when stranger anxiety emerges; separation anxiety occurs in the first year or two of life (Beesdo, Knappe, & Pine, 2009; Gullone, 2000). In contrast to anger, which shows linear increases through early childhood, fear typically only increases linearly over the first several years of life. Then, fear typically begins to plateau in early childhood (Braungart-Rieker, Hill-Soderlund, & Karrass, 2010). Of note, this developmental cascade of distinct fears is observed across cultures, suggesting that it reflects evolutionarily determined, core features of human maturation.

Although, on average, fear and anxiety follow the normative developmental trajectory described earlier, there is considerable variability in normal levels of fear and anxiety over the course of development (Braungart-Rieker et al., 2010). It is normal, for example, for children to experience transient increases in levels of fear and anxiety following major life events (e.g., the birth of a sibling, parental distress, moving to a new home). Moreover, the appropriate level of fear and anxiety in response to new situations may depend highly on the child's environment (i.e., whether the child's environment is safe and predictable and provides nurturance and support in the context of threat).

Even outside of these external factors, however, there is normal variability in levels of fear that infants and children experience. Some of this variability is captured by the notion of temperament, which may be defined as early-appearing, trait-like individual differences in emotional, attentional, and motor reactivity to novel stimuli (Rothbart, 2007). Temperaments associated with children's fearful behavior are moderately stable from the preschool period through childhood and into adulthood. Typically, the correlations among measures of temperament over childhood are in the .3 to .4 range (Fox, Henderson, Rubin, Calkins, & Schmidt, 2001; Gest, 1997; Kerr, Lambert, Stattin, & Klackenberg-Larsson, 1994), which means that temperament is somewhat less stable than the most stable individual-difference measures assessed during this time period, such as aggression (Alink et al., 2006).

Some individuals have a temperament that includes a negative, fearful reaction to novel stimuli. Although these individuals are at increased risk for anxiety disorders (discussed in more detail below), their fear is not defined as rising to the level of an anxiety disorder unless it is associated with significant distress or functional impairment. Thus, two considerations go into differentiating normal from abnormal fear and anxiety. One factor concerns the level of distress. Anxiety disorders differ from normal fears and anxieties based on the associated high level of distress, which typically persists for weeks. Because this distinction involves considerable subjective judgment from the clinician, anxiety disorders are more easily differentiated from normal fears by the second distinguishing characteristic, impairment, which refers to fear or anxiety that prevents the child from performing age-expected functions that are performed by peers. An example of such impairment might be avoidance, such as refusing to separate from a parent or attend various activities.

DSM-5 operationalizes these two considerations to define anxiety

disorders as "disorders that share features of excessive fear and anxiety and related behavioral disorders" (American Psychiatric Association, 2013). Of note, judgments regarding excessiveness involve assessments by the clinician of developmental level; high levels of anxiety considered atypical in a 4-year-old may be considered normal in a 2-year-old child. Although DSM-5 lists 11 different types of anxiety disorders, by far the most research in preschool samples pertains to separation anxiety disorder (SAD), social phobia (SOC), generalized anxiety disorder (GAD), and specific phobia (SPEC). Of note, DSM-IV also included obsessive–compulsive disorder (OCD) and posttraumatic distress disorder (PTSD) in the anxiety disorders. However, DSM-5 separates these and related conditions, which are not reviewed in this chapter, into new categories: "obsessive–compulsive and related disorders" for OCD and "trauma- and stressor-related disorders" for PTSD. Key symptoms and duration criteria for the four anxiety disorders covered in this chapter are listed in Table 6.1. Notably, most of the research on preschool anxiety disorders performed to date has used DSM-IV (or even DSM-III) rather than DSM-5 criteria. Other than a few wording changes for SAD and the reclassification of OCD and PTSD, however, the core features of pediatric anxiety disorders discussed in this chapter are unchanged between DSM-IV and DSM-5. Accordingly, studies using DSM-IV criteria are applicable for DSM-5 diagnoses.

As with other psychiatric illnesses, anxiety disorders may be expressed in a developmentally modified fashion in preschool samples relative to older children and adults. A primary difference is that preschool children may not express subjective feelings of fear or anxiety for specific stimuli (e.g., separation in SAD or dogs in SPEC). Instead, preschool children may express their anxiety primarily through behavior, such as avoidance, crying, anger, freezing, or clinging. In fact, anxiety disorders in preschoolers may be underrecognized, because some anxiety symptoms may be misinterpreted as defiance, irritability, or oppositionality. The reported prevalence rates of preschool anxiety disorders range broadly from 1.5% (Wichstrøm et al., 2012) to 22.2% (Paulus, Backes, Sander, Weber, & Von Gontard, 2015). Egger and Angold (2006b) have argued that some of this variability (see below) may be a result of misclassifying anxiety disorders as disruptive behavior disorders, such as oppositional defiant disorder (ODD); the distinction can be difficult unless caregivers and clinicians are attuned to the specific situations in which a preschooler is becoming irritable or disruptive. In addition to differences in expression of fear and anxiety, a few other modifications are made in the criteria for anxiety disorders in children versus adults. Most of these differences are related to number of symptoms required to meet criteria for a specific disorder, such as GAD, for which children require fewer symptoms to meet criteria for the disorder. This difference at least partially reflects the greater difficulty in symptom ascertainment among children than adults.

By considering specific features of individual anxiety disorders, several studies suggest that DSM-5 accurately captures the clinical picture associated with preschool anxiety disorders. Prior to these studies, there was significant concern that preschoolers' emotions were too undifferentiated to be classified

TABLE 6.1. Major Symptoms of Separation Anxiety Disorder, Social Phobia, Generalized Anxiety Disorder, and Specific Phobia

Disorder	Key symptoms	Duration criterion
SAD	• Excessive distress when experiencing or anticipating separation from caregiver • Excessive worry about losing a caregiver or about harm to them • Excessive worry about an untoward event causing separation from a caregiver • Reluctance or refusal to go out because of fear of separation from caregiver • Excessive fear about being alone in one's home or other setting • Reluctance or refusal to sleep away from home without being near caregiver • Repeated nightmares concerning separation from caregiver • Repeated complaints of physical symptoms upon actual or anticipated separation	4 weeks
SOC	• Excessive fear or anxiety in one or more social situations • Symptoms must occur in peer settings, not just around adults • Child fears he or she will act in a way that will result in negative evaluation • The feared social situation(s) almost always elicit fear or anxiety • The feared social situation(s) are avoided or endured with great distress • The fear is out of proportion to the actual danger posed by the social situation	6 months
GAD	• Excessive worry or anxiety about multiple events or activities • Difficulty controlling the worry • Associated with one of the following: restlessness, fatigue, difficulty concentrating, irritability, muscle tension, difficulty sleeping	6 months
SPEC	• Excessive fear about a specific object or situation • Feared object or situation almost always elicits fear • Feared object or situation is actively avoided or endured with great distress • Fear or anxiety is out of proportion to actual danger	6 months

as discrete anxiety disorders, along the same lines as adult anxiety disorders; that preschoolers' anxiety, compared to anxiety in older individuals, would be more nonspecific, transient, or not clearly identifiable as crossing the clinical threshold in the context of normative peaks in anxiety. Empirical data have shed light on these issues over the last decade. Spence, Rapee, McDonald, and Ingram (2001), Strickland et al. (2011), and Edwards, Rapee, Kennedy,

and Spence (2010) all examined the structure of preschool anxiety symptoms in large community samples. Spence et al. (2001) had mothers (n = 755) and fathers (n = 383) report on their preschoolers' symptoms of anxiety. Strickland et al. (2011) used diagnostic interviews in the parents of 796 4-year-olds, and Edwards, Rapee, Kennedy, and Spence (2010) used a parent questionnaire to assess anxiety symptoms in 1,182 children ages 3–5 years. All of these studies tested several models regarding how symptoms of anxiety disorders could cluster, from simple one- or two-factor models that lumped most anxiety symptoms together into a single disorder, up to four- and five- factor models that follow the current DSM classification system. Each of these studies found evidence that current DSM classification best captures the patterns of symptom clusters found in the community compared to other, less-differentiated models. Eley et al. (2003) and Sterba, Egger, and Angold (2007) similarly used large samples of preschoolers and reported that, in general, differentiated models along the lines of DSM-IV outperformed less differentiated models, although Sterba et al. (2007) did not find clear evidence for separating GAD from major depressive disorder.

ASSESSMENT

Many different methods can be used to assess symptoms of anxiety disorders during the preschool period. Some of the most commonly used measures are listed in Table 6.2 and include a variety of parent or teacher report symptom questionnaires, structured or semistructured diagnostic interviews with the parent, and laboratory observational measures. Each method has advantages and disadvantages, making multi-informant and multimethod assessments preferred whenever possible. Symptom questionnaires are the least expensive and least burdensome to participants. However, such methods are subject to various forms of informant bias. For example, ratings can be influenced by the informants' own psychopathology or misperception of the child's behavior and emotional state. Moreover, informants may have difficulty rating the child relative to population norms. Diagnostic interviews allow a clinician to help clarify and anchor symptoms, but these interviews require more time, interviewer expertise, and an informant attuned to the child's potential psychopathology. In epidemiological studies, interviews often involve high levels of structure, so that the procedures typically used by a clinician can be applied to a limited degree by a lay interviewer. This type of interview has been called either a "highly structured" or "lay" interview. Highly structured interviews enable a level of standardization that can be deployed in research but typically cannot be used as a stand-alone measure in the clinic. In the epidemiological studies reviewed below, the Preschool Age Psychiatric Assessment (PAPA) is the most frequently employed interview.

Ideally, assessment of the child includes information gleaned from direct interaction with the child. In older children and adults, assessments involve extensive discussions with the patient. However, preschool children's immature

TABLE 6.2. Commonly Used Assessment Tools for Preschool Anxiety Disorders

Parent questionnaires

- Child Behavior Checklist/1.5–5 (CBCL; Achenbach & Rescorla, 2001)
- Child Symptom Inventory (CSI; Gadow & Sprafkin, 1994)
- Preschool Anxiety Scale—Revised (PAS-R; Edwards, Rapee, Kennedy, et al., 2010)

Diagnostic interviews

- Preschool Age Psychiatric Assessment (PAPA; Egger & Angold, 2006b)
- Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS; Birmaher et al., 2009)
- Development and Well-Being Assessment (DAWBA; Goodman et al., 2000)
- Anxiety Disorder Interview Schedule (ADIS; Silverman & Albano, 1996)

Observational measure

- Anxiety Dimensional Observation Scale (Anx-DOS; Mian et al., 2015)

cognitive state complicates direct assessment. Direct laboratory observations of children in structured settings (e.g., having a stranger enter the room) have the advantage of not depending on the reliability of parent or teacher report (Mian, Carter, Pine, Wakschlag, & Briggs-Gowan, 2015), but may depend on the child's mood on the day they are assessed and may therefore fail to capture the child's emotional state over more extended periods. Other approaches rely on props, such as puppets, to elicit reports from the child. Finally, as illustrated in Figure 6.1, temperament assessments and related clinical procedures expose children to standard fear-inducing scenarios (or scenarios designed to induce other mood states) in a controlled environment, so that standard observations can be recorded. Despite the advantages and disadvantages of each measure, these measures generally are correlated with each other, and each can predict functional difficulties. As discussed earlier, best practices utilize a multimodal assessment, although this practice is not always feasible. Moreover, as this is an emerging area of science, variability continues to exist across the many techniques for integrating multimodal information to generate diagnoses in individual children.

PREVALENCE

Many studies have attempted to estimate the prevalence of anxiety disorders during the preschool period (Bufferd, Dougherty, Carlson, & Klein, 2011; Earls, 1982; Egger & Angold, 2006b; Franz et al., 2013; Keenan, Shaw, Walsh, Delliquadri, & Giovannelli, 1997; Lavigne et al., 1996; Lavigne, Lebailly, Hopkins, Gouze, & Binns, 2009; Martín, Granero, & Ezpeleta, 2014; Paulus et al., 2015; Petresco et al., 2014; Wichstrøm et al., 2012). A subset of these studies and prevalence estimates are listed in Table 6.3. Note that many of the earlier studies were described in detail in the previous edition of this handbook

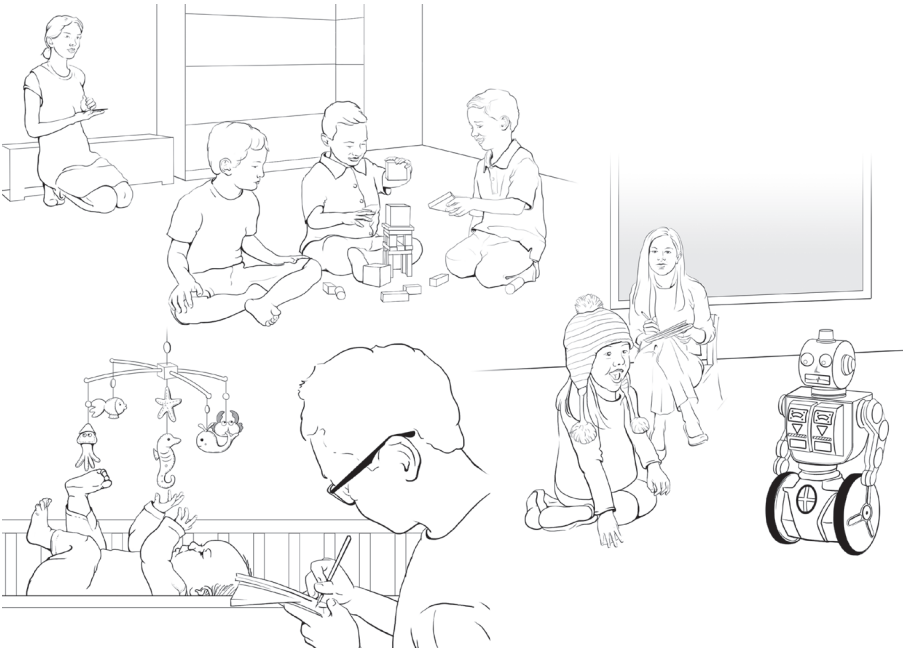

FIGURE 6.1. Standard scenarios used to evaluate children's temperament and anxiety include presentation of new toys and social interactions with unknown peers.

(Egger & Angold, 2006a). At least three large studies of prevalence of anxiety disorders in the United States have been reported since the publication of this previous edition. Lavigne et al. (2009) recruited a sample of 796 children at an average age of 4.4 years from primary care sites and public preschools near Chicago, Illinois. Parents were interviewed using the Diagnostic Interview Schedule for Children—Young Child Version (DISC-YC) to evaluate for GAD and the Child Symptom Inventory to evaluate for GAD and SAD; SOC and SPEC were not evaluated. Bufferd et al. (2011) recruited a community sample of 541 children of average age 3.6 years from near Stony Brook, New York. Parents were interviewed with the PAPA, and children underwent observational measures of temperament. Franz et al. (2013) screened 3,433 children between ages 2 and 5 years near Durham, North Carolina, using 10 items from the Child Behavior Checklist (CBCL). The 944 children who screened high for anxiety plus an additional 189 random children who did not screen high were invited to participate in the full study. Of these children, 917 participated in the full study, and parents were interviewed using the PAPA. Prevalence estimates were weighted to account for the screen-stratified sample.

These and other recent studies of preschool psychopathology in the United States provide reasonably consistent estimates of prevalence of preschool anxiety disorders. Bufferd et al. (2011) reported the prevalence of preschool

TABLE 6.3. Prevalence of Preschool Anxiety Disorders in Community Samples

Study	Location	Measure	Ages	*N*	Any anxiety disorder	SAD	SOC	GAD	SPEC
Earls (1982)	Martha's Vineyard, MA	Clinical interview	3 years	100	—	5.0	2.0[a]	—	—
Lavigne et al. (1996)	Cook County, IL	Clinical consensus	2–5 years	510	—	0.5	0.7[a]	—	0.6
Keenan et al. (1997)	Allegheny County, PA	K-SADS	5 years	104	—	2.3	4.6	—	11.5
Egger & Angold (2006)	Durham County, NC	PAPA	2–5 years	307	9.4	2.4	2.1	3.8	2.3
Lavigne et al. (2009)	Cook County, IL	DISC-YC CSI	3–5 years	796	—	0.6 2.1	—	 3.9	—
Bufferd et al. (2011)	Stony Brook, NY	PAPA	3 years	541	19.6	5.4	4.4	3.9	9.1
Gleason et al. (2011)	Bucharest, Romania	PAPA	1.5–5 years	350	4.5	1.3	0.6	2.5	0.3
Wichstrom et al. (2012)	Trondheim, Norway	PAPA	4 years	995	1.5	0.3	0.5	0.0	0.7
Franz et al. (2013)	Durham County, NC	PAPA	2–5 years	917	19.4	10.5	7.5	8.6	—
Martin et al. (2014)	Barcelona, Spain	DICA-PPYC	3 years 5 years	622 537	7.7 11.7	2.1 1.3	1.9 3.6	0.1 0.5	3.6 8.3
Paulus et al. (2015)	Southwest Germany	CBCL and DISYPS-II	4–7 years	1,342	22.2	7.0	10.7	3.4	9.8
Petresco et al. (2014)	Pelotas, Brazil	DAWBA	6 years	3,585	8.8	3.2	0.1	0.2	5.4

Note. SAD, separation anxiety disorder; SOC, social phobia; GAD, generalized anxiety disorder; SPEC, specific phobia; PAPA, Preschool Age Psychiatric Assessment; DISC-YC, Diagnostic Interview Schedule, Young Children; CSI, Child Symptom Inventory; DICA-PPYC, Diagnostic Interview for Children and Adolescents for Parents of Preschool and Young Children; DAWBA, Development and Well-Being Assessment; K-SADS, Kiddie Schedule for Affective Disorders and Schizophrenia; CBCL, Child Behavior Checklist; DISYPS-II, Diagnostik-System für psychische Störungen nach ICD-10 und DSM-IV für Kinder und Jugendliche–II.

[a]Prevalence of avoidant disorder, using DSM-III criteria.

anxiety disorders at 19.4%, while Franz et al. (2013) reported 19.6%; Lavigne et al. (2009) did not assess all anxiety disorders and did not provide an overall prevalence estimate. These three studies provided prevalence estimates for SAD from 3.9 to 10.5%, for SOC from 4.4 to 7.5%, and for GAD from 0.6 to 8.6%. The lower estimates tended to derive from the Lavigne et al. study, which notably used a different diagnostic interview (DISC-YC) compared to the other studies (PAPA). The DISC-YC relies heavily on parental response, whereas the PAPA utilizes interviewer anchoring of symptoms.

Several additional studies, including many outside the United States, have also assessed the prevalence of childhood psychopathology. These studies have reported estimates of the prevalence of anxiety disorders that vary considerably, from 1.5% (Wichstrøm et al., 2012) to 22.2% (Paulus et al., 2014), with most studies citing prevalence between 10 and 20%. Similar variability exists in prevalence estimates of individual anxiety disorders, as can be seen in Table 6.3. Variability in prevalence estimates is likely the result of considerable heterogeneity across studies including geographical location (Wichstrøm et al., 2012), method used to ascertain the diagnosis of an anxiety disorder (Lavigne et al., 2009), demographic differences between samples, and so forth. One of the largest sources of variability is likely related to differences in thresholds for making the diagnosis of an anxiety disorder, because adjusting the level of impairment required to make the diagnosis has been found to alter prevalence rates significantly (Egger & Angold, 2006b).

Prevalence estimates in epidemiological studies outside of the United States appear somewhat lower than those in the United States. It is unclear whether these differences reflect true regional differences or differences in methodology. Wichstrøm et al. (2012) examined a screen-stratified population sample of 995 children from Norway using the PAPA and elicited a prevalence of 1.5% for all anxiety disorders combined. Martín et al. (2014) used a screen-stratified community sample of 622 and evaluated preschoolers at age 3 using a semistructured interview, the Diagnostic Interview for Children and Adolescents for Parents of Preschool and Young Children (DICA-PPYC), and reported a prevalence of 7.7%. Petresco et al. (2014) utilized a birth cohort in Brazil of 1,342 children at a mean age of 6.1 years, interviewed parents with the Development and Well-Being Assessment (DAWBA, a structured interview), and reported a prevalence of 8.8%. Gleason et al. (2011) examined a screen-stratified sample of children obtained from outpatient waiting rooms in Bucharest, Romania, with the PAPA and reported a prevalence of 4.5%. Finally, Paulus et al. (2015) used a set of questions from the CBCL and the DISYPS-II (a German symptom questionnaire) and reported a prevalence of 22.2% for anxiety disorders in preschoolers in Southern Germany. Prevalence rates for specific anxiety disorders are listed in Table 6.3.

Despite variability in estimates of prevalence across studies, most epidemiological studies in preschoolers that assess for a range of psychiatric disorders find that anxiety disorders are the most prevalent class of psychiatric disorders (Petresco et al., 2014), consistent with epidemiological studies in older children and adults. Moreover, prevalence estimates do not vary much from

the preschool period to the early school age in studies that examine prevalence in both age groups (Bufferd, Dougherty, Carlson, Rose, & Klein, 2012). The highest estimates of anxiety disorders in adolescents and adults are around 30% (Kessler et al., 2005; Merikangas et al., 2010), and such high rates are as likely to reflect methodological features as they are true population differences in prevalence. Retrospective studies of older children suggest that the median age of onset of anxiety disorders is around 6 years of age (Merikangas et al., 2010); this estimate is likely to be biased toward older ages given the difficulty of obtaining an accurate retrospective report. Taken together, these data suggest that anxiety disorders are the most common form of psychiatric disorder across the lifespan; that anxiety disorders tend to start very young; and that the prevalence of anxiety disorders is relatively stable, around 20%, across the lifespan.

Interestingly, most studies of preschool anxiety disorders do not find any difference in prevalence estimates of anxiety disorders across sex (Dougherty et al., 2013; Gleason et al., 2011; Lavigne et al., 2009; Petresco et al., 2014; Shamir-Essakow, Ungerer, & Rapee, 2005) or ethnicity (Dougherty et al., 2013; Hudson, Dodd, Lyneham, & Bovopoulous, 2011; Lavigne et al., 2009), although occasional sex differences have been reported (Franz et al., 2013; Gleason et al., 2011; Paulus et al., 2015). These findings stand in contrast to studies in older children and adults that do report increased rates of anxiety disorders in females compared to males (Kessler et al., 2005; Merikangas et al., 2010). Interestingly, although there are no consistent differences in prevalence estimates of anxiety disorders in male versus female preschoolers, the expression of anxiety disorders may vary with sex in the preschool period. In the large epidemiological study by Bufferd et al. (2011) discussed earlier, boys with anxiety disorders were more inhibited than boys without anxiety disorders, whereas girls with anxiety disorders were more *dis*inhibited than girls without anxiety disorders. Boys with anxiety disorders also had less exuberance than girls with anxiety disorders. In addition, some studies have reported increased anxiety *symptoms* and increased rates of anxious temperament associated with anxiety disorders (Dougherty et al., 2011) in preschool females relative to preschool males; although other studies find no sex differences in symptoms either (Edwards, Rapee, & Kennedy, 2010). Taken together, these studies suggest that although there may be differences in the expression and symptoms of anxiety in males versus females, differences in actual prevalence of anxiety disorders do not emerge until after the preschool period.

Epidemiological studies have also characterized comorbidity patterns. In general, preschoolers with anxiety disorders, relative to their peers without anxiety disorders, are more likely to have other anxiety disorders (Bufferd et al., 2011; Paulus et al., 2014), depression (Bufferd et al., 2011), attention-deficit/hyperactivity disorder (ADHD; Lavigne et al., 2009), and ODD (Bufferd et al., 2011; Lavigne et al., 2009; Martín et al., 2014). Among preschoolers with an anxiety disorder, about 25–30% have more than one anxiety disorder (Bufferd et al., 2011; Dougherty et al., 2013; Franz et al., 2013). In

a study of 854 preschool-age twin pairs, Eley, Rijskijk, Perrin, O'Connor, and Bolton (2008) assessed anxiety disorders with the Anxiety Disorder Interview Schedule (ADIS) and reported that the comorbidity between SAD and SPEC was explained by shared environmental influences, while the comorbidity between SOC and SPEC was a result of both familial and nonshared environmental influences. From 30 to 50% of preschoolers with anxiety disorder have some other nonanxiety psychiatric disorder (Franz et al., 2013). This shared risk likely is related to a combination of genetic and environmental influences (Silberg et al., 2015). Studies of autistic spectrum disorders that include children in the preschool age range have reported substantially increased rates of GAD relative to children without autism (Salazar et al., 2015).

Preschool anxiety disorders may be associated with significant functional impairment. In the Bufferd et al. (2011) sample, both categorical diagnosis of an anxiety disorder and dimensional symptom counts of anxiety on the PAPA were linked to lower functioning, as assessed with the Vineland and the Children's Global Assessment Scale (association between diagnosis and Vineland was not significant). In the Franz et al. (2013) sample, the impact of preschool anxiety disorders was measured with the Child and Adolescent Impact Assessment. Families of children with anxiety were 3.5 times more likely to report that children's behavior had a negative impact on family, even after researchers controlled for other illnesses. GAD and SAD impacted family relationships, while SOC resulted in restriction in activities. Anxiety disorders tend to be less impairing, however, relative to ODD (Martín et al., 2014) and depression (Towe-Goodman, Franz, Copeland, Angold, & Egger, 2014). Anxiety disorders that are comorbid with depression (Von Klitzing et al., 2014) or ODD (Martín et al., 2014) are more functionally impairing relative to pure anxiety disorders. Von Klitzing (2014) evaluated 236 children with the PAPA and reported that children with comorbid anxiety and depression had worse functional impairment, more family adversity, more maternal depressive symptoms, worse family environment, and more family conflict relative to preschoolers with anxiety disorders alone.

RISK FACTORS

Numerous risk factors have been associated with preschool anxiety disorders. One observation has been that preschoolers with anxiety disorders are more likely to have parents with anxiety disorders or related forms of psychopathology. The number of anxiety disorders in preschool children is correlated with maternal anxiety (Shamir-Essakow et al., 2005), and preschoolers with anxiety disorders are more likely to have a mother who had an anxiety disorder in the preceding month relative to peers without an anxiety disorder (Dougherty et al., 2013). Furthermore, parental history of depression increases risk for all preschool anxiety disorders (Dougherty et al., 2013) and is associated with increased symptoms of anxiety disorders (Hopkins, Lavigne, Gouze,

Lebailly, & Bryant, 2013). Edwards, Rapee, and Kennedy (2010) assessed anxiety in a community sample of 638 three- to 5-year-old children with the Preschool Anxiety Scale—Revised (PAS-R), a parent-report questionnaire. Parents additionally reported on their own negative affect by completing the 21-item Depression, Anxiety and Stress Scale (DASS-21). Edwards et al. (2010) detected a significant relation between preschool anxiety and maternal negative affectivity. Beyond parental psychopathology, various other factors also have been linked to preschool psychopathology, including medical conditions in the child. For example, Rogers, Lenze, and Luby (2013) examined 306 children and reported that children born late preterm had higher rates of anxiety disorders, as assessed by the PAPA, relative to children born full term. The relationship between prematurity and preschool anxiety disorders, furthermore, was mediated by maternal history of depression.

Parental psychopathology may be related to anxiety disorders in preschoolers through several different mechanisms, including direct genetic transmission of risk, parenting practices, observation of parental anxiety, or other pathways. Given that most assessments rely heavily on parental reports, biased reporting also could be a factor, producing an artificial elevation in rates. Theoretical work suggests that children acquire fears through direct experience with threatening stimuli, witnessing others experience threatening stimuli, and through verbal transmission of information about potential threats (Rachman, 1991). Empirical evidence suggests that children learn to fear and avoid stimuli about which they are told negative information (Field & Lawson, 2003), consistent with verbal transmission.

Several studies have used genetically informative designs in an attempt to disentangle contributions to anxiety disorders in preschoolers through genetic or environmental effects. Eley et al. (2003) examined anxiety symptoms in 4,564 twin pairs using a parental questionnaire and reported that heritability for specific anxiety symptoms was in the moderate range, from 39% for separation anxiety symptoms to 64% for shyness symptoms. Shared environmental influences ranged from 3% for shyness symptoms to 35% for separation anxiety symptoms. Similarly, Silberg et al. (2015) examined a sample of 312 Puerto Rican twin pairs and used the DISC-YC to assess for SAD. This group reported that additive genetic factors accounted for 28% of the variance in SAD, while shared environmental factors accounted for 15% of the variance. Note that these heritability estimates are somewhat lower than heritability estimates for other psychiatric disorders, including autism, schizophrenia, ADHD, and bipolar disorder (McGrath, Weill, Robinson, Macrae, & Smoller, 2012). This difference may suggest that anxiety disorders are somewhat more strongly related to environmental and experiential factors relative to other forms of psychopathology. However, other explanations also are possible. For example, lower reliability in ratings of anxiety compared to other forms of psychopathology also could produce the observed patterns of findings.

Other family-based factors have been linked to preschool anxiety. For example, data suggest that preschoolers with younger, poorer, less-educated

parents are more likely to have anxiety disorders, as compared to preschoolers with older, more financially secure, or better educated parents. Specifically, preschoolers with an anxiety disorder are more likely to have parents that did not graduate from college relative to peers (Dougherty et al., 2013). Lower family income is a risk factor for both SPEC (Bufferd et al., 2011) and overall anxiety symptoms (Hopkins et al., 2013) during the preschool period (but see Petresco et al., 2014). Children with SAD tend to have younger fathers relative to peers (Bufferd et al., 2011), and preschoolers living with both biological parents have lower rates of generalized anxiety disorder compared to preschoolers who do not (Franz et al., 2013). Preschool anxiety disorders have also been associated with having more siblings in the household (Franz et al., 2013), and preschoolers in homes with more family conflict are more likely to have anxiety symptoms than preschoolers in homes with low levels of conflict (Hopkins et al., 2013). As discussed earlier, these findings may reflect either environmental or genetic influences. For example, shared genes could influence both the chance that anxious parents attend college and the chance that an anxious parent will have anxious children. Alternatively, aspects of parenting practices, differences in overall household stress, or some combination of these or other factors could directly contribute to preschool anxiety. Randomized controlled trials attempting to change parenting and genetically informative observational studies could clarify which of these possibilities may be more likely. Finally, it has been reported that preschoolers with anxiety disorders are more likely to have experienced a recent stressor compared to peers (Dougherty et al., 2013; Edwards, Rapee, & Kennedy, 2010), suggesting that stress plays at least a partial role.

Another line of work examines associations between parenting styles and risk for preschool anxiety disorders. As with the risk factors discussed earlier, it is not clear whether certain parenting styles *cause* anxiety disorders, whether preschoolers with anxiety disorders *elicit* certain parenting behaviors, whether there are shared genetic effects, or some other factors. Nevertheless, it is thought that the best parenting style for a preschooler with an anxiety disorder is an empathic, firm, and in-control style, which encourages exposure to fear. Specifically, this type of parent gently but firmly encourages his or her child to overcome fears though gradual exposure, while at the same time empathizing with any feelings of distress. Dougherty et al. (2013) examined parenting behaviors in the Stony Brook study described earlier through a combination of observational parent–child interactions and parent questionnaires. In addition to authoritative (high warmth, high control), Dougherty et al. also rated parents as authoritarian (low warmth, high control) and permissive (high warmth, low control). Parents of children with anxiety disorders were observed to be less supportive; mothers of preschoolers with anxiety disorders rated themselves as more authoritarian and permissive; while fathers of preschoolers with anxiety disorders rated themselves as more permissive (Dougherty et al., 2013). Lewis-Morrarty et al. (2012) found similar associations among early childhood temperament, parental behavior, and risk for adolescent anxiety.

Many researchers have reported a particular relation between overprotective parenting and preschool anxiety disorders (e.g., Edwards, Rapee, & Kennedy, 2010; Hudson et al., 2011; Vreeke, Muris, Mayer, Huijding, & Rapee, 2013). In theory, overprotective parenting may be related to anxiety because preschoolers might not get the opportunity to master their fears. When a child is shielded from feared stimuli and discouraged from coping directly with it, the child may implicitly learn that the best way to manage his or her anxiety is to avoid the feared stimuli, which actually serves to reinforce avoidance as a coping skill and prolong the anxiety disorder. Consistent with this hypothesis, preschoolers with anxiety disorders are less likely to go to preschool compared to children in the same age group without anxiety disorders (Dougherty et al., 2013). Interestingly, these effects of parenting may manifest very early in life, as the normal linear increase in fear seen from 4 months to 12 months of age is slower in infants whose mothers are more sensitive to their children (Braungart-Rieker et al., 2010).

Another closely related line of work pertains to the link between attachment and preschool anxiety disorders. "Attachment" is defined as the bond between a child and parent. A secure parent–child attachment permits the child to explore the world, while also having the ability to return to a safe, reliable base. Some forms of insecure attachment are theorized to result in anxiety because the preschooler cannot rely on a predictable caregiver to provide a safe haven. Consistent with this hypothesis, Shamir-Essakow et al. (2005) reported a link between insecure attachment and number of anxiety disorders in the preschool period. Other results during the preschool period have been mixed. Brumariu and Kerns (2010) performed a systematic review of studies examining the link between attachment and symptoms of anxiety, and found some evidence for the hypothesis that attachment security is associated with lower levels of anxiety in children and adolescents, although results were more consistent during the adolescent period. Lewis-Morrarty and colleagues (2015) found that attachment interacts with other early-childhood risk factors, such as temperament, in predicting later risk for anxiety disorders.

Beyond parent factors, one of the most frequently identified risk factors for preschool anxiety disorders is temperament. As mentioned earlier, "temperament" may be defined as early-appearing, trait-like individual differences in emotional, attentional, and motor reactivity to novel stimuli (Rothbart, 2007). "Behavioral inhibition" (BI) is a temperament characterized by high negative reactivity to new stimuli, especially social stimuli. A wealth of evidence suggests that high behavioral inhibition temperament in early childhood is associated with risk for anxiety disorders, especially social anxiety disorder, later in childhood and in early adulthood (Clauss & Blackford, 2012; Rapee, 2014). Dougherty et al. (2013), in the Stony Brook sample, examined the temperaments of BI and also positive affectivity (PA) and negative affectivity (NA). Preschool children with anxiety disorders had higher BI and lower PA relative to children without anxiety disorders; no differences were detected in NA between groups. Other studies have similarly reported that BI is associated

with the diagnosis of an anxiety disorder (Paulus et al., 2015; Vreeke et al., 2013) and the number of anxiety disorder diagnoses (Shamir-Essakow et al., 2005) during the preschool period. Other studies have reported links between preschool anxiety disorders and variation in other aspects of temperament, including high fear, low sociability, and low exuberance (Dougherty et al., 2011); and negative affect and lower effortful control (Hopkins et al., 2013). A study of 312 Puerto Rican twin pairs suggested that the link between BI and SAD is due to genetics (Silberg et al., 2015). One challenge in studies relating temperament to anxiety disorders, however, is high overlap between characteristics of specific temperaments such as BI and symptoms of anxiety disorders (Egger & Angold, 2006b). Longitudinal studies that incorporate measures of temperament before the onset of anxiety disorders may address some of these confounds.

Some recent work suggests that specific temperaments may be related to risk for specific preschool anxiety disorders. Dyson, Klein, Olino, Dougherty, and Durbin (2011) used a series of laboratory observational measures to separately define "social" and "nonsocial" BI by coding children's reactions to social and nonsocial stimuli, respectively. Interestingly, these two measures were not correlated with each other. Social BI was related to symptoms of social anxiety disorder and separation anxiety, as assessed by the PAPA, while symptoms of SPEC were related to nonsocial BI. GAD was not related to either form of BI.

IMPACT OF PRESCHOOL ANXIETY DISORDERS BEYOND THE PRESCHOOL YEARS

A critical issue is whether there are meaningful differences in the life trajectory of children with preschool anxiety disorders relative to nonanxious peers. We review below the few studies that have longitudinally examined the relation between preschool anxiety disorders and symptoms later in the preschool period, in early childhood, and adolescence. The majority of these studies relate preschool anxiety to anxiety during early school age; much less is known about the influence of preschool anxiety later in childhood and beyond. The available literature suggests that preschool anxiety is a powerful predictor of early school-age anxiety, with odds ratios ranging from 3 to 60 for individuals' anxiety disorders at age 3 years predicting anxiety disorders at age 6 years (Bufferd et al., 2012). Nevertheless, the majority of preschool children, about 60%, recover from their anxiety disorder by early school age (Battaglia et al., 2015). Many more studies are needed, however, to understand fully the impact of preschool anxiety disorders both during childhood and into adulthood. Developmental studies in other domains suggest that the impact of early life events may not be evident until much later in life (Maurer, Mondloch, & Lewis, 2007). Therefore, it is critical to follow individuals with anxiety during the preschool period into adulthood, even if symptoms are not manifest during later childhood and adolescence.

A couple of studies with short follow-up periods have examined the trajectory of anxiety symptoms within the toddler-to-preschool period and support modest-to-strong continuity. Overgaard et al. (2014) characterized 628 children at ages 18 months and 3.5 years of age with the CBCL and the PAPA. Anxiety symptoms at age 18 months were significantly but modestly (odds ratio 1.41) associated with anxiety at age 3.5 years. Edwards, Rapee, and Kennedy (2010) utilized a community sample of 638 three- to 5-year-old children and had their parents fill out the PAS-R, as well as a range of other questionnaires at baseline and 12 months later. Anxiety symptoms over 12 months were highly stable, with correlations in anxiety measures around .75. In addition to anxiety at baseline, anxiety 12 months later was predicted by BI, maternal negative affectivity, and parental overprotection at baseline, as well as impact of negative life events.

A number of studies have examined the relation between preschool anxiety and anxiety in early school age, as well as specific risk factors associated with continuity of anxiety over this short time interval (Battaglia et al., 2015; Bufferd et al., 2012; Danzig et al., 2013; Hudson et al., 2011; Kearney, Sims, Pursell, & Tillotson, 2003). These studies have examined both "homotypic" continuity, which is continuity of the same disorder over time, and "heterotypic" continuity, which refers to one disorder (e.g., SAD) predicting symptoms of another disorder (e.g., SOC). Bufferd et al. (2012) and Danzig et al. (2013) both examined continuity of anxiety symptoms from ages 3 to 6 in the Stony Brook epidemiological study described earlier. In this sample, anxiety disorders as a group and each individual anxiety disorder (except GAD) exhibited significant homotypic continuity (Bufferd et al., 2012). Odds ratios for anxiety disorders at age 3 predicting anxiety disorders at age 6 years were 2.87 for SPEC, 7.88 for SAD, and 60.14 for SOC. In addition, there was significant heterotypic continuity among the anxiety disorders, and SAD at age 3 years predicted depression, ODD, and agoraphobia at age 6 years (Bufferd et al., 2012). Danzig et al. (2013) examined the functional impact of the continuity of symptoms and reported that anxiety symptom counts on the PAPA at age 3 predicted low popularity and shyness at age 6, even when accounting for symptoms of ODD, ADHD, and depression. These effects appeared to be mediated by anxiety symptoms at age 6 (Danzig et al., 2013).

Other studies examining trajectories of anxiety symptoms from the preschool period into early school age support the hypothesis of continuity of symptoms through this time interval. Kearney et al. (2003) used the Anxiety Disorders Interview Schedule for DSM-IV—Child and Parent Versions (ADIS-IV-C/P) and examined a relatively small group of 44 children in a longitudinal study at average ages 3 years and 6.5 years. Of the nine children who had SAD at age 3, two still had SAD at age 6.5 years, five had subclinical SAD, and two were in nonclinical status. Children who had comorbidity with other psychiatric disorders or a family history of anxiety disorders were more likely to have continued symptoms at age 6.5 years. Battaglia et al. (2015) examined symptoms of SAD using a subset of questions from the CBCL in

1,933 children at six separate time points from ages 1.5 years to 6 years. They found that 6.9% of children had high symptoms of SAD at young ages that steadily increased over the preschool period, while 10.8% of all children had high SAD symptoms early on that largely abated by age 6 years. These data suggest that most children with initial high symptoms in preschool resolve by the beginning of school age, but a significant minority exhibit continuity. The high, increasing trajectory was associated with maternal depression, parental unemployment, and maternal smoking during pregnancy. Continuity versus discontinuity of anxiety symptoms from the preschool period into early school age likely depends on many factors, including genetic risk, temperament, and environment. To disentangle these effects, Hudson et al. (2011) performed comprehensive assessments in a longitudinal group of 178 children at ages 4 and 6 years. Child temperament was assessed with the Short Temperament Scale and laboratory observational measures. Anxiety disorders were measured by using the ADIS-IV-P, and anxiety symptoms were measured with the PAS-R. In addition to the predicted relation between anxiety at 4 and 6 years of age, anxiety disorders and symptoms at follow-up at 6 years of age were also predicted by BI, maternal anxiety disorder, maternal overinvolvement, and maternal negativity at baseline. Notably, only BI and maternal anxiety disorder predicted anxiety at age 6 when accounting for anxiety at baseline.

Relatively few studies longitudinally examine the trajectory of preschool anxiety symptoms beyond early school age, although available extant data again support modest continuity. Pihlakoski et al. (2006) evaluated the same group of children at age 3 and age 12, and assessments included parental report via the CBCL. Internalizing symptoms at age 3 were significantly related to internalizing symptoms at age 12 but only in girls, and symptoms at age 3 explained just 12% of the variance at age 12. Broeren, Muris, Diamantopoulou, and Baker (2013) performed a 2-year longitudinal study on a community sample of 224 children, ages 4 to 11 years, and measured anxiety symptoms with the PAS-R. They used growth mixture modeling to identify the developmental trajectory of symptoms of major anxiety disorders. Interestingly, symptoms of SAD and SOC were relatively stable across ages 4 to 11; so children high in these anxiety symptoms at age 4 were predicted to have the same level of high anxiety at age 11 years. Consistent with these studies, stably high SAD and SOC symptoms were associated with a temperament of high BI, as measured with the Behavioral Inhibition Questionnaire. In contrast to SAD and SOC, however, there were two trajectories of GAD symptoms, each with a different shape. One trajectory was stably low from ages 4 to 11 years, while the other steadily increased from age 4 up to a peak at age 8; in this case, symptoms at age 4 did not differentiate the two different trajectories of symptoms. A drawback of this study is the relatively short follow-up period, so most of the trajectories had to be inferred from cross-sectional relations. Nonetheless, this study and others support low-to-modest continuity and highlight the need for further studies with longer longitudinal follow-up.

In contrast to research on preschool anxiety disorders, a substantial literature exists regarding relations between preschool temperament and anxiety outcomes in later childhood and adolescence. As described earlier, this literature supports a robust relation between the early childhood temperament of BI and social anxiety disorder later in life (Clauss & Blackford, 2012; Rapee, 2014). A recent meta-analysis of seven high-quality studies reported that risk of developing social anxiety disorder is over seven times greater in individuals with a history of high versus low levels of BI (Clauss & Blackford, 2012). Given this robust relation, clinicians should consider behaviorally inhibited temperament as one of the most potent preschool-age predictors of developing an anxiety disorder later in life.

Taken altogether, several tentative conclusions can be reached regarding continuity of preschool anxiety disorder into later life. First, preschoolers with anxiety disorders appear to be at significantly elevated risk for developing anxiety disorders later in life relative to preschoolers without anxiety disorders. Despite this increased risk relative to peers, however, *the majority* of preschoolers with anxiety disorders *will not* have an anxiety disorder later in life. Several factors, including child temperament and parenting styles, as described earlier, may predict which children with preschool anxiety disorders will have continued symptoms into later childhood and beyond. Finally, more work is needed to characterize continuity of preschool anxiety disorders to anxiety symptoms later in life; a much larger literature supports a relation between the temperament of BI during the preschool period and later development of an anxiety disorder.

NEUROBIOLOGY

Although there is a substantial literature regarding the neurobiology of anxiety disorders in older children and adults, relatively little is known about the neurobiology of anxiety disorders in preschoolers. Of note, the data reviewed earlier suggest that the prevalence of preschool anxiety disorders is quite high and approaches rates seen in older samples (Merikangas et al., 2010) and preschool anxiety is continuous with anxiety later in life. Accordingly, this gap in the literature is problematic. Because of the known genetic, temperamental, and early environmental risk factors, the etiology of many or most anxiety disorders almost certainly involves the developmental neurobiology of the preschool period (Pine, 2007), and further studies are required.

Animal and human studies of older children and adults support a model of anxiety disorders that includes pathologically increased activity in brain regions that evaluate and signal threats in the environment. This increased activity is coupled with decreased functioning of brain regions that are thought to regulate this activity. Brain regions involved in identifying and signaling threat include the amygdala, hippocampus, hypothalamus, the bed nucleus of the stria terminalis, the ventral tegmentum, and numerous other brain stem nuclei (LeDoux, 2000; Tovote, Fadok, & Lüthi, 2015). Regions involved in

regulating this threat- and fear-related circuitry include the medial prefrontal cortex, the dorsolateral prefrontal cortex, and the ventrolateral prefrontal cortex (Blackford & Pine, 2012; LeDoux, 2000; Sylvester et al., 2012; Tovote et al., 2015). Different regulatory brain regions may be involved in different phenomenological aspects of fear and anxiety regulation such as habituation, cognitive reappraisal, or orienting attention away from feared stimuli.

A substantial body of work supports the hypothesis that orienting attention away from feared stimuli is an important regulator of fear (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van IJzendoorn, 2007), and the neural circuitry underlying this form of fear regulation appears to include the dorsolateral and ventrolateral prefrontal cortex (Blackford & Pine, 2012; Pine, Guyer, & Leibenluft, 2008; Sylvester et al., 2012). A couple of studies suggest that this important regulation mechanism is present in the preschool period. Braungart-Rieker et al. (2010) examined 143 mother–infant dyads at child ages 4, 8, 12, and 16 months. Higher levels of fear were noted in infants who looked more at potentially threatening stimuli, instead of gazing at other, more neutral, stimuli. Similarly, Hopkins et al. (2013) reported that high effortful control was associated with decreased preschool symptoms of anxiety disorders. One possible explanation is that higher effortful control enables preschoolers to orient attention to the task at hand rather than toward feared stimuli. Future studies are needed to detect the underlying neurocircuitry involved in orienting attention toward or away from feared stimuli in preschoolers.

One study of brain activity during the preschool period does support the hypothesis that variation in brain activity is related to preschool anxiety disorders similar to adults. Meyer, Hajcak, Torpey, Kujawa, Kim, et al. (2013) used electroencephalography (EEG) to measure the error-related negativity (ERN) in 48 6-year-old children with anxiety disorder versus 48 6-year-old children without anxiety disorder. Consistent with a large body of work in older children and adults, preschoolers with an anxiety disorder had a larger ERN compared to controls. The ERN is thought to index activity in the dorsal anterior cingulate and several other brain regions following commission of errors. This activity may be increased in anxiety disorders, because making an error may be perceived as threatening in some way.

Although there are very few studies of brain activity in preschoolers with active anxiety disorders, a couple of studies have demonstrated an enduring impact of preschool anxiety disorders on brain function into adolescence. Although more studies are needed to replicate and extend these findings, these studies provide initial evidence that preschool anxiety disorders may be an early maker of altered brain development. Sylvester et al. (2013) used functional magnetic resonance imaging (fMRI) to demonstrate that children with a history of past anxiety disorders (most occurring during the preschool period) had decreased functional connectivity between brains regions involved in orienting attention. Carpenter et al. (2015) utilized subjects from the Duke Preschool Anxiety Study mentioned earlier (Franz et al., 2013) and measured brain activity with fMRI in a subset of 45 children between ages of 5.5 years

and 9.5 years. Carpenter et al. (2015) noted that children with preschool anxiety disorders had specific differences in dorsolateral prefrontal cortex activity and amygdala functional connectivity relative to children with no prior history of an anxiety disorder. The specific connections affected varied depending on whether children had had SAD, SOC, or GAD, suggesting that the long-term impact on brain function may depend on the particular anxiety disorder during the preschool period.

Measures of sympathetic activity such as heart rate and skin conductance provide indirect measures of brain activity, especially the brain's response to stress. A series of studies has provided evidence of increased sympathetic reactivity in preschool children with anxious temperaments (e.g., BI) in response to novelty (Fox, Henderson, Marshall, Nichols, & Ghera, 2005; Kagan, 2002; Scarpa, Raine, Venables, & Mednick, 1997). Additional studies incorporating more direct measures of brain activity are required to clarify the neurobiological basis of this increased sympathetic response to novelty.

TREATMENT

Treatments for preschool psychiatric disorders are covered extensively in Part III of this handbook. Therefore, we briefly highlight only the major trends in treatment of preschool anxiety disorders here.

There are several evidence-based psychotherapy options for preschool anxiety disorders that should be considered first-line treatments. Similar to therapy in older age ranges, many studies support the use of cognitive-behavioral therapy (CBT) for preschool anxiety disorder (Donovan & March, 2014; Freeman et al., 2014; Hirshfeld-Becker et al., 2010; Monga, Young, & Owens, 2009; Schneider et al., 2011). Most adaptations of CBT during the preschool period include significantly more involvement of the parent compared to CBT used in older age groups. Benefits of parental involvement include aiding communication with the therapist, reinforcement of therapeutic interventions at home, reduction in parental anxiety, improvement in parenting responses to child anxiety, and increased parental self-confidence. Along these lines, there is evidence that adaptations of parent–child interaction therapy (PCIT) that explicitly address parenting issues in addition to child-specific interventions work in treatment of preschool anxiety disorders (Carpenter, Puliafico, Kurtz, Pincus, & Comer, 2014; Comer et al., 2012). Some studies demonstrate improvement in preschool anxiety disorders with parenting interventions alone (Kennedy, Rapee, & Edwards, 2009).

Another approach has been to try to prevent preschool anxiety disorders by addressing risk factors gleaned from the studies described earlier. These studies have shown initial promise in preventing preschool anxiety disorders. In theory, these interventions could correct the altered trajectory of brain function associated with preschool anxiety disorder described earlier, though this correction has not been shown. Rapee, Kennedy, Ingram, Edwards, and

Sweeney (2010), for example, devised an intervention for preschoolers with high BI that included parenting skills training, cognitive restructuring, and exposure. Children who received the intervention (n = 73) had fewer anxiety disorders up to 36 months later compared to children in a monitoring-only group who did not (n = 73).

Many fewer and much smaller studies support the use of medication for preschool anxiety disorders. In general, since CBT is the less invasive treatment and has considerable data documenting efficacy, CBT typically is considered the first-line treatment for preschool anxiety disorders. Moreover, data in nonhuman primates raise some additional, specific concerns about potential long-term effects of early medication (Shrestha et al., 2014). As a result, medications should be considered second-line treatments for preschool anxiety in children who fail to respond to age-appropriate adaptations of CBT or are not candidates for treatment with CBT for various reasons. For such children who cannot receive CBT, medication does remain an option. A recent review describes 11 studies that examined the use of medication in preschool children with either depressive or anxiety disorders, and provides evidence that medications may be beneficial (Barterian et al., 2014). Based on these data, medications may be considered as a second line of treatment once psychotherapies have been tried and fail.

CONCLUSIONS

Anxiety disorders are the most common psychiatric disorders in the preschool years and across the lifespan, affecting up to 20% of children before the age of 6 years. Preschool anxiety disorders are associated with increased risk for other psychiatric disorders and can be functionally impairing. Many risk factors have been identified, including behaviorally inhibited temperament, family history of anxiety disorders, specific parenting styles (e.g., overprotection), and multiple environmental factors (e.g., recent stressors). Although most preschool anxiety disorders remit by early childhood, a significant minority of children with preschool anxiety disorders continue to experience impairment into school age and beyond. Preliminary evidence suggests that preschool anxiety disorders are associated with functional brain changes later in life, even in individuals who no longer have an anxiety disorder, suggesting that the impact of preschool anxiety disorders may extend beyond overt anxiety later in life. Fortunately, there are many evidence-based treatment options for preschool anxiety disorders, and newer treatments are being developed to prevent preschool anxiety disorders by modifying risk factors. These findings together suggest that identification and early intervention in preschool anxiety is of great importance and is now feasible, and therefore should be attended to in clinical settings. Despite this body of knowledge, much more research is required into the etiology, neurobiology, and long-term impact of treated and untreated preschool anxiety disorders.

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7

Depressive Disorders

Phenomenology and Alterations in Emotion Processing

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In this chapter, we review the available empirical data on the clinical characteristics, neural correlates, and longitudinal course of depressive disorders with onset during the preschool period of development. Historically, there has been much skepticism about the application of mood disorder diagnoses to young children, despite compelling clinical observations as early as the late 1940s of depressed affect arising in the infancy and preschool periods. Public acceptance and understanding of this clinical syndrome has steadily progressed over the last two decades in part because of accumulating empirical data from numerous national and international sites validating preschool depression (Bufferd et al., 2014; Fuhrmann, Equit, Schmidt, & von Gontard, 2014; Gaffrey, Belden, & Luby, 2011; Luby, Si, Belden, Tandon, & Spitznagel, 2009; Luby et al., 2003b; Wichstrøm & Berg-Nielsen, 2014). We review these data, as well as emerging findings that elucidate the associated alterations in emotion functioning and neurobiology. To provide the reader with a clinical picture of this disorder, we describe representative clinical cases of depressed preschoolers.

Essential to understanding early-onset depressive disorders (i.e., prior to age 6) is knowledge about the normative developmental trajectory of related basic emotional processes. Research characterizing normative extremes of

emotion development and identifying objective boundaries for when extremes are indicative of clinically relevant psychopathology remain underinvestigated in our opinion. Nonetheless, in recent years, several key findings provide ideal exemplars of research that clarify the distinction between extreme yet normative behavioral expressions of preschoolers' temper tantrums, irritability, and experiences of guilt versus clinically significant manifestations of these behaviors that cross boundaries into psychopathology (Dougherty et al., 2015). Along these lines, we also review the available empirical database and its substantial gaps related to the typical emotional development of joy and sadness and their regulation, as well as the "complex and self-conscious" emotions of guilt and shame. These selected emotions are deemed key to understanding the developmental psychopathology of depressive disorders, but they are complicated by extreme variation in expression, understanding, and regulation, especially during the preschool period of development. We also review developmental literature on "emotion dynamics" and "emotional competence," and describe how these developmental trajectories are altered in preschool-onset depression.

DEPRESSIVE DISORDERS IN THE PRESCHOOL PERIOD

The Idea of Depressive "Disorder" in a Young Child

The concept of clinical depressive disorders arising in young children is, in general, one that meets with strong resistance from the lay public. This may be because it is both disturbing and counterintuitive to imagine a young child reared in the absence of major trauma or adversity, suffering from a clinical mood disorder. The notion of an early-onset depression conflicts with the wish that early childhood be an inherently joyful and carefree time of life. Furthermore, the normative extremes of emotional experiences and the intense emotional responsivity known in early childhood create greater ambiguity in our efforts to distinguish clinical disorders from normative and transient developmental difficulties. Due to the unfortunate social stigma that continues to surround mental disorders, it is important to avoid prematurely or inaccurately labeling young children with diagnosis of a depressive disorder. With that said, given mounting evidence of the neurodevelopmental nature of depressive disorders, there is no reason to rule out a mood disorder based on age alone. Findings have indicated that many parents of depressed preschoolers started observing depressive symptoms in their child before age 2 (Luby & Belden, 2012). Given the potential for more effective intervention earlier in life (see Part III, this volume), related to greater neuroplasticity of the brain during this period (see Troller-Renfree & Fox, Chapter 1, this volume), it is equally important to identify affective disturbances that cross the clinical threshold or serve as markers of risk for impairing depressive disorders at the earliest possible developmental period. Therefore, although the issue of normative developmental variation (i.e., extreme behaviors, but

still within the developmentally "typical" range) must be considered, available data inform the critical distinctions between the normative and transient emotional difficulties of development, and clinically significant signs and symptoms of depression (Belden, Thomson, & Luby, 2008; Dougherty et al., 2013, 2015; Luby et al., 2003b).

History of Observations and Investigation of Depressive Affect Early in Life

As early as the mid-1940s, the behaviors and emotional expressions of infants with a presumed depressive syndrome were described by pediatrician Renée Spitz. Spitz was among the first to identify remarkable alterations in affective expressions observed in human infants separated from their primary caregivers and maintained in institutional settings. These observations represent the first and earliest identification of the expressions of depressed mood and related negative affect in human infants, and contradicted prevailing developmental theory suggesting that it was impossible for these emotions to be experienced at this early developmental point. These observations were also consistent with psychoanalytic theory proposing that "anaclitic depression" could arise in infancy as a response to separation from the caregiver (Spitz, 1945, 1946, 1949).

Despite these compelling observations, Spitz's publications had little impact on the practice of mainstream child psychiatry or child development research for many decades, until interest in high-risk studies of the infants of depressed mothers was initiated in the early 1980s. These studies, which set the groundwork for later clinical investigations of depression in young children, focused on normal and aberrant development of mood and affect in infants and toddlers at "high risk" for depression on the basis of having a depressed mother. "High-risk" studies utilized standardized observations of the infant offspring of mothers experiencing mood disturbances compared to the offspring of healthy mothers. This approach was compelling, based on the known increased rate of affective disorders in the offspring of individuals with mood disorders (Feng et al., 2012; Kovacs, Devlin, Pollock, Richards, & Mukerji, 1997; Pilowsky et al., 2014; Silk et al., 2011; Weissman et al., 1984, 1996, 1999).

Although Spitz focused on samples of institutionalized children experiencing emotional deprivation, these studies had clear implications for a greater understanding and appreciation of the complexity of the early emotional experience of normally developing young children. Since the time of Spitz's observations, research in developmental psychology has begun to investigate empirically the expression of emotions in infancy and early childhood. Despite the renewed and ongoing interest in the role of emotion in early child development, gaps in the literature about the normal development of specific emotions and associated emotional regulatory processes remain.

Phenomenology of Depression in Preschoolers

Age-adjusted criteria for the identification of clinical depression in young children between ages 3 and 6 years was described and validated from two independent study samples in St. Louis (Luby, Belden, Pautsch, Si, & Spitznagel, 2009; Luby et al., 2002, 2003a). More recently, preschool depression has been identified and distinguished from other disorders in numerous independent samples in the United States and Europe (Bufferd et al., 2014; Wichstrøm & Berg-Nielsen, 2014). Empirical studies of preschool depression were built on the foundation of the numerous early case studies and data from smaller samples suggesting that a depressive syndrome might be identifiable in preschool children (e.g., Kashani, 1983; Kashani & Carlson, 1985; Kashani, Holcomb, & Orvaschel, 1986; Kashani & Ray, 1983; Kashani, Ray, & Carlson, 1984). Kashani et al. (1986) studied the third edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III; American Psychiatric Association, 1980) symptoms of depression in community samples of preschoolers and identified "concerning symptoms" but few children who met formal criteria for major depressive disorder (MDD), which suggested the need for developmental modifications to the depression criteria for preschoolers.

Subsequently, Luby et al. (2002b, 2003) demonstrated that the "typical" symptoms of MDD could be identified in preschool children when symptom states were "translated" to describe age-appropriate manifestations of DSM MDD constructs. One tangible and straightforward example of this was the description of anhedonia as "the inability to enjoy activities and play." A further developmental modification they tested was that persistent negative themes in play were considered as an age-adjusted manifestation of a depressive symptom in lieu of (or in addition to) direct expression of sadness, guilt, persistent negative thoughts, and negative self-perceptions. In addition, depressed preschoolers displayed psychomotor signs such as fatigue, alterations in sleep and appetite, as well as agitation. Taken together, numerous findings supported the notion that the basic integrity of the core depressive constructs (the adult manifestation of which are described in the DSM system) appeared to manifest as early as age 3 when age-appropriate questions were asked of caregivers. This finding refuted early prevailing developmental theory suggesting that young children would manifest "masked" symptoms of depression (e.g., somatic symptoms and/or aggression) instead of depressed affect. Similar to findings from investigations of this issue in older depressed children, we found that masked symptoms appeared in depressed young children, but with much less frequency than "typical" symptoms such as sadness, irritability, or vegetative signs, in addition to changes in activity, sleep, and appetite (Carlson & Cantwell, 1980; Luby, Belden, Pautsch, et al., 2009; Luby et al., 2003b).

The sign/symptom of anhedonia emerged as a characteristic of a more severe and putative melancholic subtype in young children (Luby, Mrakotsky, Heffelfinger, Brown, & Spitznagel, 2004). Furthermore, anhedonia also

emerged as a highly specific symptom of depression (and was not observed in any child in the psychiatric or healthy comparison groups). Preschoolers with depressive symptoms characterized by anhedonia had greater depression severity, greater alterations in cortisol reactivity, and failure to brighten in response to joyful events, similar to characteristics demonstrated in adults with this depressive subtype. This distinction may be important for future treatment studies of young children, because melancholic depressed adults appear to have unique treatment responses (Klein, 1974). The notion that an inability to experience pleasure and joy from activities and play would be a clinical symptom in a preschooler and a marker of serious psychopathology is inconsistent with the concept that young children are inherently joyful and pleasure seeking. Therefore, impairments in the young child's ability to experience joy and pleasure could be a marker of a clinical problem. In keeping with this concept, preschoolers were more likely to appear, and to describe themselves, as "less happy" rather than overtly "sad" than were same-age nondepressed peers (Luby et al., 2002). Consistent with this, and perhaps a more reliable marker, was that decreased response to reward and to joyful stimuli has been detected in acutely depressed compared to healthy preschoolers using event-related potentials (Belden et al., in preparation).

The symptom of "pathological guilt" has also emerged as a key marker of preschool depression. Pathological guilt is characterized by having a very low threshold for experiencing guilt after a transgression (Luby, Belden, Sullivan, et al., 2009). This may manifest as feelings of guilt about something for which the child is not even responsible. Another manifestation of pathological guilt is becoming preoccupied with guilt and being unable to recover from it, sometimes for hours or even days. Children may express this symptom by repeatedly asking for reassurance (e.g., "Do you still love me?"), or forgiveness, or by becoming withdrawn and sad even after a minor transgression. Alternatively, children may inappropriately insist that things are their fault. Importantly, preschool-onset guilt was associated with a smaller anterior insula measured at school age, a region of the brain in which guilt processing takes place (Belden et al., 2015). Having a smaller anterior insular volume was then a predictor of later depression recurrence in middle childhood. Based on this, guilt may be an important early marker and target for intervention in preschoolers' depressive disorders.

Another common manifestation of depressive symptoms in preschool-age children is pessimism characterized by persistent and unrealistic feelings and expressions that they will never achieve a desired goal. Preoccupation with death, expressed verbally or in play themes (the latter to the exclusion of all other themes) may also be an important marker. Changes in sleep, appetite, or energy level, as well as mood-related cognitive disturbances and intense and frequent irritability and sadness are also common features (Dougherty et al., 2013). The presence of neurovegetative signs in these very young depressed children was evidenced by the finding that 80% of depressed preschoolers showed changes in sleep, 80% had weight or appetite changes, and 71%

demonstrated changes in levels of physical activity. Regarding the "masked" symptoms or "depressive equivalents" mentioned earlier, 51% had multiple somatic complaints, and only 37% of depressed preschoolers displayed the more nonspecific symptom of regression in development (Luby et al., 2002; see Figure 7.1). Also of importance, to distinguish depression from other early-onset disorders, symptoms such as guilt, anhedonia, diminished cognitive abilities, and fatigue may be used as highly specific symptoms (Luby, Belden, Sullivan, et al., 2009; see Table 7.1).

The expression of suicidal ideation (SI), both passive and active, may also be present, as well as suicidal gestures, such as wrapping things around the neck or threatening to jump from high porches or into traffic. While the exact meaning of these expressions in children this young remains unclear, and it may be a more general expression of intense distress, the symptom shows stability over time and therefore does not appear to be a transient and spontaneously resolving preoccupation (Whalen, Dixon-Gordon, Belden, Barch, & Luby, 2015). Future studies are needed to determine whether SI in preschool-age children is related to familial or media exposures, and whether and to what extent these children understand the permanence of death. Despite the lack of clarity on the meaning of these expressions and behaviors, they must be taken seriously, and appropriate action should be taken to ensure the safety

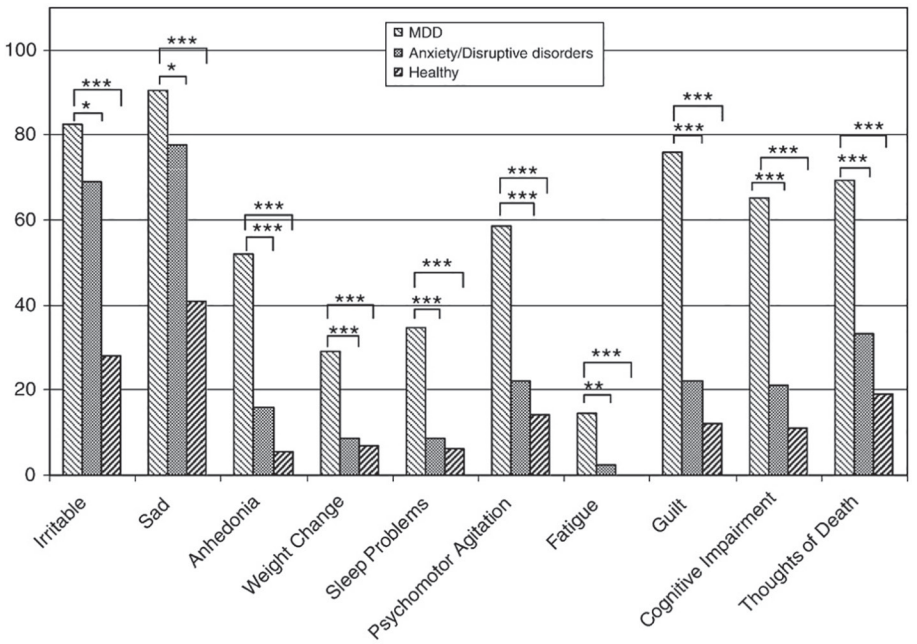

FIGURE 7.1. Percent of PAPA MDD symptoms endorsed across the three diagnostic groups. ***$p < .001$; **$p < .01$; *$p < .05$.

TABLE 7.1. Odds Ratios for MDD Diagnosis on MDD Symptoms Controlling for Anxiety and Disruptive Disorders

	Irritable	Sad and/or tearful	Anhedonia	Weight change	Sleep problems	Psychomotor agitation	Fatigue	Guilt	Diminished cognitive abilities	Thoughts of death
Anxiety	2.36**	2.52*	1.76	0.89	1.5	1.08	1.38	1.55	1.27	1.31
Disruptive	3.23***	3.39***	1.36	0.6	0.61	1.71	1.28	1.16	1.55	3.12***
MDD	4.03***	5.22***	8.39***	6.84***	7.56***	5.55***	15.93***	14.95***	9.32***	4.81***

***$p < .001$; **$p < .01$; *$p < .05$.

of the child. Furthermore, even if they do not represent a serious intent to self-harm, the longitudinal stability of these expressions suggests they may serve developmentally to instantiate the idea of self-harm as a coping response, which could become a threat to safety later in life.

The signs/symptoms of anhedonia and pathological guilt (in addition to or in combination with other key symptoms discussed earlier) appear to be useful screening items for depression in large populations (Luby, Heffelfinger, Koenig-McNaught, Brown, & Spitznagel, 2004). To screen for depression in preschool-age children, the Preschool Feelings Checklist (PFC; Luby, Heffelfinger, Mrakrotsky, & Hildebrand, 1999), a 16-item yes–no questionnaire, is suitable for use in primary care or other community-based settings; it has established reliability, as well as favorable specificity–sensitivity balance (Luby et al., 2004). A score of 3 or greater on the checklist suggests that further clinical evaluation for a mood disorder is warranted. The feasibility and public health benefit of screening for depression in primary care settings has been well established in older children (e.g., Asarnow et al., 2005).

Risk Condition or Clinical Syndrome?

An issue of some controversy in studies of preschool depression, related to some of the principles outlined earlier, is whether depression arising in preschoolers represents a risk state or a clinically significant disorder. While some depressed preschoolers may meet all DSM criteria for MDD, it is more typical for young children to have shorter durations of episodes (parents do not often report that children have sustained symptoms for 2 weeks or longer) and those who meet four instead of the five DSM criteria also have the clinical markers described earlier and the neurobiological markers described below. Based on this, those who fail to meet full criteria might be more accurately classified as having "minor depression." However, importantly, they do present as both impaired and distressed, a key feature of the clinical definition of a "case" (Luby, Belden, Pautsch, et al., 2009). In addition to clinically significant levels of impairment and distress, results from this laboratory and others indicate that "at-risk/acutely ill" depressed preschoolers consistently and reliably function differently from typical peers in emotional, social, and cognitive domains based on teacher, caregiver, and interviewer reports, as well as when observed during objective observational tasks conducted in a controlled laboratory setting. Findings from a longitudinal study of depressed preschoolers who have been followed into later school age reveal that preschool-onset depression is a robust marker for meeting full DSM-5 criteria for depression in later childhood, even after accounting for other key risk factors (Luby, Gaffrey, Tillman, April, & Belden, 2014). Therefore, it is clear that these children are at very high risk for having a later, full-blown major depressive episode. Based on this, clinical identification and early intervention is clearly warranted, regardless of whether the preschool syndrome is viewed as a clinical or high-risk state.

Neurobiological Correlates

Establishing biological mechanisms (precursors, correlates, and/or outcomes) is a key element in the validation of a psychiatric disorder. Along this line, several investigations have established that the known biological markers in depressed adults can also be detected in depressed preschoolers. Preschool children between the ages of 3 years and 5 years, 11 months show alterations in cortisol reactivity in response to psychosocial stress, consistent with elevations in stress hormones reactivity ("stress response gone awry") known in adult depression (Luby et al., 2003a). Perhaps more importantly, a number of researchers have now investigated school-age children with a history of preschool depression who have similar alterations in brain function and structure as those established in depressed adolescents and adults (Barch, Gaffrey, Botteron, Belden, & Luby, 2012; Foti, Kotov, Klein, & Hajcak, 2011; Luking et al., 2011; Suzuki et al., 2013). School-age children with a history of preschool depression show thinning of the ventromedial prefrontal cortex (vmPFC), decreases in volume and thickness of whole-brain cortical grey matter across middle childhood, and smaller anterior insula volumes (Belden et al., 2015; Luby et al., 2016; Marrus et al., 2015). These changes in brain structure, previously found in depressed adults, have now been detected as early as middle childhood in subjects with a history of preschool depression, suggesting that alterations in the structure of brain regions involved in emotion processing and regulation are neurodevelopmental in origin and can be identified early in life.

Several researchers have also reported alterations in brain function in response to viewing negative stimuli, as well as connectivity of networks implicated in the cognitive control of emotions (a.k.a. "emotion regulation") in school-age children with a history of preschool depression (Barch et al., 2012; Gaffrey, Luby, et al., 2011; Luking et al., 2011). Furthermore, Gaffrey, Barch, Singer, Shenoy, and Luby (2013) conducted task-based functional imaging in acutely depressed preschool children and demonstrated the same increase in amygdala reactivity to negative emotion known to characterize depressive states in depressed adults. All of these findings together strongly support the notion that preschool depression is characterized by alterations in psychophysiology (i.e., EEG and hypothalamic–pituitary–adrenal [HPA] axis), aberrations in the function and structure of brain regions, as well as connectivity within/between networks that subserve emotion reactivity and regulation, all of which are known to be altered in adult depression. Therefore, it seems this early-onset disorder has a surprisingly similar neurobiological profile and is likely an early manifestation of the well-established disorder in adults.

Case Descriptions

A 3-year, 6-month-old African American female was referred to the infant/preschool mental health clinic by her day care teacher due to sustained nonparticipation in activities, isolated play, and social withdrawal.

She was described as having a "flat" and "serious" mood both at home and at school. Although she did not appear to enjoy school, she did not display separation anxiety. Her behavior at home and at school was also described as very slow; it took an excessively long time for her to complete a task. Although no weight loss was noted, her disinterest in food and snacks was also evident in the school setting. A sustained preoccupation with negative play themes was also described by her mother and observed on clinical evaluation. She had no medical illness or notable developmental delay. A further family history revealed extensive anxiety and mood disorders in first- and second-degree relatives.

A 4-year-old European American male expressed on a daily basis that he wanted to kill himself in response to frustration. He was also very pessimistic about his ability to accomplish goals and had a very negative self-image ("No one likes me" and "I'll never be good at that") that was resistant to reassurance or experiences of success. He tended to take responsibility for things that went wrong at home, repeatedly stating, "I'm sorry, please don't be mad at me," even when things were not his fault. He was disruptive in school, had few friends, and could also be aggressive with older siblings at home. His biological father, with whom he had only infrequent contact, had a history of depression and suicidality.

EMOTIONAL DEVELOPMENT AND MOOD DISORDERS

We have demonstrated in the previous sections that data on the phenomenology of preschool depressive disorders defining their characteristics and distinguishing them from normative emotional extremes are now available. However, the finer details of developmental manifestations of emotions and mood during this period remain important areas for future research. Future investigations must account for two critical developmental issues. The first is whether sufficient emotional development has taken place for the specific mood symptoms to manifest. The second issue is the need to distinguish between normative difficulties of emotional development and clinically significant phenomena. This task is complicated by the presence of major gaps in the empirical literature in the area of preschool emotional development pertinent to mood disorders. In an attempt to elucidate some of these issues, we provide in this section a brief review of the development of emotions pertinent to mood disorders.

Defining "Emotion"

Emotions are a rich and complex part of the human experience, and their role in intrapsychic, interpersonal, and social functioning is of paramount importance to understanding developmental psychopathology in general and mood disorders in particular. However, defining "emotion" is a surprisingly

difficult task. Emotion is a construct that seems to elude definition, without invoking a related construct or synonym (e.g., feeling or affect). Despite this, emotion itself is a universal human experience, the meaning of which is self-evident. Most standard definitions describe the sources, outcomes, and correlates of emotion but seemingly fail to capture the essence of what qualifies as a true emotion. The functionalist approach to emotion development outlines the useful and cogent rationale that emotions serve to create, preserve, or disrupt relations between an individual and his or her internal and external environment, when such relations are deemed significant (Campos, Mumme, Kermoian, & Campos, 1994; Fridja, 1986).

Normative Developmental Trajectory of Emotion States Pertinent to Mood Psychopathology

Our ability to define and understand early mood psychopathology is inextricably linked to and limited by our understanding of the normative development of basic, as well as complex, emotions related to mood disorders, such as joy, sadness, guilt, and shame. Whereas previous investigators (e.g., Kochanska, Gross, Lin, & Nichols, 2002; Tangney, Wagner, & Gramzow, 1992) have examined the development of complex emotions such as guilt and shame, there is a dearth of investigations on the normative experiences and expressions of basic emotions, such as joy and sadness, during the preschool period. Surprisingly, gaps in the emotion development literature pertaining to the experience of basic emotions during the preschool years remain despite the many useful frameworks and theoretical approaches to emotion development that have been proposed but remain insufficiently empirically tested (Campos et al., 1994; Sroufe, 1996, 1997; Thompson, 1990, 1991).

A Brief Overview of the Development of Joy, Sadness, Guilt, and Shame

The Development of Joy

Previous emotion research examining the development of joy has focused on children from birth to approximately 2 years of age. For example, observational studies of facial expression have shown that the human infant begins to express joy and happiness during the first 6–8 weeks of life (White, 1985). Social smiles during interaction with caregivers during this period mark the infant's first expressions of joy. Shortly after their first social smiles, infants begin to show happiness in both social and nonsocial contexts when they are able to manipulate a particular event or object (Lewis, Alessandri, & Sullivan, 1990). At 7 months, infants begin to smile and laugh while interacting with familiar adults. As children mature cognitively, they begin to take pleasure (as evidenced by increased smiling and laughing) in unexpected or discrepant events (e.g., in response to a funny noise or face) (Kagan, Lapidus, & Moore, 1978).

Research on the experience and expressions of joy in older children often emphasizes their ability to recognize joy in self and others, explains the causes of joyful feelings, and examines children's expressions of joy. For instance, by 2 years of age, children are able to amuse themselves and become interested in their ability to elicit laughter from others. At 3 years of age, children begin to report feelings of joy in response to gratifying experiences (Denham & Zoller, 1991). For instance, young children may report being joyful when playing at the park or when a parent gives them a special toy or treat. Children between 3 and 7 years of age also report physical stimuli (e.g., being tickled or receiving hugs) as a source for joy (Denham & Zoller, 1991). Starting around age 3, children begin to recognize ways to maintain feelings of joy and happiness. For example, young children often report knowing that because physical and social aggression can cause feelings of happiness to change to sadness, aggression is to be avoided to maintain positive affect (McCoy & Masters, 1985).

The Development of Sadness

Izard, Hembree, and Huebner (1987) found that sadness can be reliably differentiated from other negative emotions in the human infant as early as 2 months of age, detected by inference from facial expressions. Between ages 2 and 6 months, facial expressions of sadness arise, congruent with negative incentive events, providing further evidence for the presence of sorrowful emotion at this early point in development (Izard et al., 1995). Bowlby (1980) theorized that, related to the development of attachment, sadness that arises during the first 2 years of life is most commonly due to prolonged periods of separation from primary caregivers. Starting at around 4 years of age, children begin to experience sadness as a result of more complex social events. For example, children between 4 and 12 years of age reported the loss of relationships, the occurrence of undesirable events, experiences of powerlessness, or the possibility of being harmed as reasons for their feelings of sadness (Denham & Zoller, 1991).

By 4 years of age, children begin to demonstrate an ability to regulate their feelings of sadness. This is evidenced by the findings that during this period children often suggest that physical nurturing (i.e., receiving/giving hugs or kisses) is helpful in reducing their own, as well as others', feelings of sadness (Denham, 1998). In one of the few studies explicitly examining the development of sadness, Rotenberg, Mars, and Crick (1987–1988) found that younger children typically take an egocentric approach to explaining sadness. Specifically, young children most frequently reported sadness being caused by harm to one's self, whereas older children were more able to recognize that harm to others was also a cause for sadness. An increase in the child's sophistication in the understanding of emotions is also evidenced by children's increased awareness and understanding and perception of motives for emotions. For example, older children were more likely to understand the motives

of emotion as attempts to get others to understand their point of view (Rotenberg et al., 1987–1988).

Developmental changes in the intensity of the emotional experience of sadness with increasing age may also be present. Rotenberg et al. (1987–1988) found a trend for young children to report less intense experiences of sadness. Interestingly, children of all ages report infrequently verbalizing their sadness to others, and often do not show their sadness at all. This is in keeping with the clinical observation and empirical evidence of depressed young children reporting themselves as "less happy" rather than as overtly "sad" on an age-appropriate puppet interview (Luby et al., 2002). These findings suggest that young children may have more subtle manifestations of sadness. We have posited that this greater subtlety may contribute to decreased recognition of depressed mood states in young children.

The Development of Guilt and Shame

Emotions that require the ability to make the distinction between the expectations (i.e., goals, motivation, and behaviors) of self and others are referred to as "self-conscious" and/or "complex" emotions (Tangney et al., 1992). Young children's self-evaluations of performance in relation to the social standards and the expectations of others are prerequisites for the emotions of guilt and shame (Parisette-Sparks, Bufferd, & Klein, 2015). The development of these emotions may be of particular interest for understanding early-onset mood psychopathology, because they are core features of mood disorders in adult populations (for review, see Malti, 2016). Self-conscious emotions such as guilt and shame are salient in depressive states and theoretically could also be important in manic states if absent or occurring at low levels. Although the ability to experience complex emotions requires more sophisticated cognitive processes paired with advancing social skills, more recent data suggest that children as young as 2 years old have the ability to experience an array of complex emotions, including self-conscious emotions (Zahn-Waxler & Robinson, 1995). Using narrative techniques, Zahn-Waxler, Cole, and Barrett (1991) have shown that children as young as 3 years of age understand and experience guilt.

The clinical depression literature based on studies of older populations links depression to the chronic tendency to make internal, stable, and global self-blaming attributions (i.e., guilt and shame) in the face of negative events (Robins & Block, 1988). However, the role and salience of guilt and/or shame in depression in young children remains underexplored. Young children's ability to regulate their expression of intense positive and negative emotions, such as sadness and joy, as well as the complex emotions of guilt and shame, is an important factor in the boundary between adaptive expressions of these emotions and maladaptive expressions that cross the threshold into "symptom states." For example, preschool children with the inability to control the intensity or duration of their feelings of sadness, in addition to being prone to

experience shame and guilt, may be at much greater risk for depression compared to emotionally well-regulated, same-age peers who experience shame and guilt more rarely and only in extreme and/or appropriate circumstances.

Despite some specific data on children's experience, understanding, and expressions of joy, sadness, guilt, and shame, to date, we lack systematic literature that elucidates and tracks the normative trajectory of emotion development during the preschool period. Such information could have important clinical applications to understanding the early development of mood disorders. For instance, we do not know how often typically developing preschoolers become joyful or sad during a typical day, week, or month. The "normative" expression of guilt or shame after a wrongdoing (encompassing duration, intensity, and appropriate circumstances) remains unclear. The parameters of the healthy range and peak of intensity in a preschooler's experience and expression of joy and sadness also remain unclear. Data defining these parameters would allow clinicians to determine whether a child is falling outside of the normative range for specific emotions and crossing into the clinical range. Such data could further clarify developmental psychopathology in young children.

Emotion Regulation

In addition to the importance of understanding the normative experience and expression of specific emotions during the preschool period is the tracking of normative trajectories of young children's capacities to control and modulate their emotional expressions. Children who develop the ability to monitor, appraise, and, if necessary, modulate their emotional reactions to stimuli, allowing them to achieve goals and function appropriately within their social environments, are thought to be able to engage in effective *emotion regulation* (Campos et al., 1994; Thompson, 1994). The capacity to regulate varying intensities, durations, and specific types of emotion experiences and expressions (e.g., joy and sadness) is critical for achieving social and emotional competence, and is a key component of early emotional development (Saarni, 1999).

Previous studies examining typically developing children suggest that preschoolers who are better able to regulate inappropriate expressions of emotions, delay gratification, and use cognitive strategies to monitor their emotions and subsequent reactions tend to be more socially competent, more well-liked by peers, and are perceived as being more well-adjusted (Lemery, Essex, & Smider, 2002; Lengua, 2002). Conversely, the inability to regulate emotional experiences and expressions adaptively has been shown to place children at an increased risk for childhood psychopathology (Cicchetti, Ackerman, & Izard, 1995). Along these lines, and potentially pertinent to depressive syndromes, Zeman, Shipman, and Suveg (2002) found that school-age children's inability to regulate feelings of sadness predicted an increase in their internalizing symptoms, placing these children at a heightened risk for

psychopathology. Despite growing interest in the relationship between emotion regulation and childhood psychopathology, relatively few studies to date have addressed these constructs in a sufficiently detailed manner for application to specific clinical mental disorders.

Interventions Addressing Emotion Development

Given the importance of emotion expressivity and recognition to healthy development, it remains critical that emotion development research continue to identify whether normative emotion development trajectories are susceptible to specific environmental (e.g., caregiving, trauma) and or biological factors; that is, children's developing capacities to be emotionally aware and appropriately expressive of feelings are not only core components of socioemotional competence but also overall adaptation and mental health (Cicchetti et al., 1995; Keenan, 2000). An accumulating body of evidence suggests that when children are limited in their range of emotion expressions or are encouraged to express specific emotions to the exclusion of others, there is a greater likelihood of impaired socioemotional functioning and heighted risk for psychopathology more generally (for review, see Chaplin & Aldao, 2013; Chaplin, Cole, & Zahn-Waxler, 2005).

In recent years there has been growing awareness of the importance, malleability, and long-term effects of early emotion development on individual well-being throughout the lifespan (Domitrovich, Cortes, & Greenberg, 2007; Webster-Stratton, Reid, & Hammond, 2004). This growing recognition has spurred an increased number of classroom-based interventions specifically targeting young children's emotional competence through focused attention on enhancing emotion knowledge and development of strategies for regulating emotions. Examples of universal classroom-based prevention programs that have been successfully implemented with preschool children include Al's Pals: Kids Making Healthy Choices (Lynch, Geller, & Schmidt, 2004), the Chicago School Readiness Project (Raver et al., 2009), the Emotion-Based Prevention Program (EBP; Izard et al., 2008), I Can Problem Solve (Shure, 2001), the Incredible Years Dinosaur Classroom Curriculum (Webster-Stratton, Jamila Reid, & Stoolmiller, 2008), and the Promoting Alternative Thinking Strategies program (Domitrovich et al., 2007).

Although there was wide variation in outcome measures used to assess improvement associated with each of these prevention programs, taken as a whole, they reported improvements in children's emotional and social competence, increased capacities for problem solving, and improved overall classroom behaviors. Findings suggest that preschool children with greater emotion knowledge, and better ability to control/regulate emotion and subsequent behavioral responses to emotion feelings, experience less interference from intense positive and or negative emotion states during their day-to-day classroom routines and teacher instruction (Raver et al., 2009). It is clear that when preschool classrooms emphasize improving children's overall emotion

development, better academic, social, and behavioral outcomes are seen when compared to programs that focus solely on academic content (Blair & Diamond, 2008).

Dynamic Features of Emotion: Application to the Identification, Prevention, and Treatment of Mood Disorders

Positive and/or negative emotion arousal (e.g., joy and sadness) at appropriate or inappropriate times is thought to promote or undermine adaptive function, beginning in infancy and continuing throughout the lifespan. When an individual experiences extremes of either joy or sadness, or inappropriate joy in response to a sad event, this undermines social functioning. Mapping the dynamic trajectories of a young child's impaired emotional response gives us a novel tool to identify, quantify, and measure what may be the specific features of an individual child's emotion dysregulation leading to risk states or manifest mood disorders. This method has been used for the design of more targeted prevention and/or intervention strategies (Luby, Lenze, & Tillman, 2012). Furthermore, if, in fact, the conceptualization of this model can be operationalized, empirically tested, and validated, then "emotion reactivity curves" could potentially provide clinicians with a useful tool for understanding and assessing the unique individual features (e.g., reactivity characteristics) of mood disorder manifestations in individual children. Such an approach is currently being tested (see Elkins, Mian, Comer, & Pincus, Chapter 11, this volume for a discussion of parent–child interaction therapy and its adaptations).

CONCLUSION

An accumulating body of developmental research has provided evidence for early alterations in neurobiology and affect development in infants and preschoolers at high risk for depression, setting the stage for further studies of clinical depressive disorders in young children. Subsequently, Luby and colleagues have provided evidence that children as young as 3 years of age may display a valid clinical depressive syndrome (Luby, Belden, Pautsch, et al., 2009; Luby et al., 2002, 2003a). These data suggest that current DSM-5 criteria can be applied to preschool children when the assessment is modified to account for age-adjusted manifestations of the symptom states. Validity of the preschool depressive syndrome is now based on a large body of research on biological and neurobiological markers, adding to phenomenological work (Barch et al., 2012; Gaffrey et al., 2013; Luby et al., 2003a). In addition, evidence also suggests that there are alterations in specific aspects of emotion development that may be used as tangible treatment targets (Luby et al., 2012).

Several age-appropriate diagnostic tools are now available for the assessment of mood disorders in young children (e.g., Preschool Age Psychiatric

Assessment [PAPA]; Egger & Ascher, 1999; Kiddie-Schedule for Affective Disorders and Schizophrenia—Early Childhood Version [K-SADS-EC]; Gaffrey & Luby, 2012; Diagnostic Interview for Children—Young Child Version [DISC-YC]; Lucas, Fisher, & Luby, 1998). In addition, observational measures of emotional reactivity and parent–child relationship quality may also be very useful, as well as other measures of emotion knowledge and emotion functioning (parent–child teaching tasks; Egeland et al., 1995; Laboratory Temperament Assessment Battery [Lab-TAB]; Goldsmith, Reilly, Lemery, Longley, & Prescott, 1995; Emotion Expression Scale for Children [EESC]; Penza-Clyve & Zeman, 2002; Children's Sadness Management Scale CSMS; Zeman, Shipman, & Penza-Clyve, 2001).

We have proposed a developmental model that integrates principles of emotion dynamics and emotional competence to define the features of adaptive and maladaptive emotional reactivity during early childhood. We have proposed that the quantification and analyses of such emotional reactivity features could inform investigations of normative emotional development, as well as our understanding of the developmental psychopathology of mood disorders. We also suggest that quantitative analyses of such response characteristics might be useful for the design of targeted prevention and intervention efforts.

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8

Autism Spectrum Disorder

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Autism spectrum disorder (ASD) is a neurodevelopmental disorder whose core features of impaired social communication and atypical restricted, repetitive behaviors emerge during the preschool period. Core autistic symptoms are generally lifelong, and their relative stability, as well as their contribution to impairments in adaptive function, carry significant and devastating implications at successive stages of development. The rise in prevalence of preschool diagnoses of ASD reflects both a general rise in prevalence worldwide and earlier recognition of the syndrome when it occurs. The latter is attributable to widespread inclusion of characterizing features of the autistic syndrome in developmental screening, including early ascertainment of deficits in the capacity for protodeclarative pointing, engagement in turn-taking games, and symbolic play.

The diagnostic conceptualization of the disorder has shifted with the advent of DSM-5; language deficits, once a core feature of autism, are no longer an independent criterion domain, and Asperger syndrome and pervasive developmental disorder not otherwise specified, once subtypes of pervasive developmental disorders (PDDs), have been removed as separate diagnoses; rather most of these individuals now fall under the broader diagnostic category of "autism spectrum disorder." These changes reflect major scientific advances in knowledge about symptom structure and patterns of familial transmission in autism. Pronounced variation in autistic symptom borders, impairment in adaptive functioning (imperfectly correlated with symptom burden), and comorbidity among preschoolers affected by autism across the spectrum raise unique challenges and opportunities for comprehensive intervention planning at each stage of development. Mental health care professionals provide a key

service to families during the preschool period, because they have the opportunity to specify interventions that are tailored to a child's profile of strength and weakness, implementing whenever possible evidence-based therapies.

EPIDEMIOLOGY

Among childhood mental health conditions, ASD is notable for a steep and well-publicized rise in prevalence. ASD is a relatively recent addition to the DSM, having been introduced in DSM-III in 1980, and until a little over decade ago, was considered rare. Between 1992 and 2001, the prevalence was estimated as 12.7/10,000 (Fombonne, 2003). In the United States, the most recent prevalence estimate of 1/68 is an order of magnitude greater (Autism and Developmental Disabilities Monitoring Network Surveillance Year 2010 Principal Investigators, 2014).

Several explanations, often at the level of case ascertainment, have been proposed to contribute to this upswing in prevalence. For example, diagnostic criteria have become progressively more inclusive. DSM-5 now conceptualizes ASD as a spectrum that explicitly encompasses a range of core symptom severity, in contrast to prior definitions, which often invoked significant cognitive and language delays (American Psychiatric Association, 2013). A greater variety of standardized assessment tools, including rapid, developmental screeners that facilitate earlier detection of risk, are now available. Rising rates of research citations and media coverage support heightened awareness of ASD, both among parents and clinicians. Furthermore, "diagnostic substitution," whereby the same developmental disability receives a different diagnosis at different times (often secondary to changes in awareness or access to services), has also been implicated (Bishop, Whitehouse, Watt, & Line, 2008; Shattuck, 2006).

Throughout the diagnostic evolution of ASD, one consistent epidemiological feature has been the skewed male : female gender ratio of 4:1. Observations of quantitative trait distributions confirm this increased risk in males, which is present in the toddler period (Marrus et al., 2015). Failure to incorporate sex-specific norms in the diagnostic process has contributed to significant differences in the rates of community diagnosis for girls versus boys who manifest precisely the same level of quantitative symptom burden (Ronald, Larsson, Anckarsater, & Lichtenstein, 2014; Schaefer, Mendelsohn, & Professional Practice and Guidelines Committee, 2013; Zecavati & Spence, 2009). Furthermore, there is evidence that female sex can very often moderate the phenotypic expression of inherited susceptibility to ASD (Oono, Honey, & McConachie, 2013; Webb, Jones, Kelly, & Dawson, 2014) and that a "female protective effect" is responsible for protecting girls against the expression of inherited ASD susceptibility (Constantino & Charman, 2012; Jacquemont et al., 2014; Virkud, Todd, Abbacchi, Zhang, & Constantino, 2009).

International psychiatric epidemiological research in ASD is still emerging,

particularly in developing countries. Current global estimates suggest that the prevalence of ASD is similar throughout the world (Baxter et al., 2015; Elsabbagh, Divan, et al., 2012). A relative strength of these epidemiological studies, particularly in Sweden, involves investigations in children under the age of 7 years. One Swedish population study of 6- to 7-year-olds found a prevalence of 1.2% (Kadesjo, Gillberg, & Hagberg, 1999), while another of children age 6 years and under found a prevalence of 0.6% (Fernell & Gillberg, 2010). A report from a population in the United Kingdom, ages 5–9 years, estimated a prevalence of 1.6% (Baron-Cohen et al., 2009). These percentages are similar to a study in the United States of over 8,000 4-year-olds in South Carolina, which reported a prevalence of 0.8% (Nicholas, Carpenter, King, Jenner, & Charles, 2009). More recently, a Swedish study tracking prevalence rates of ASD in 2-year-olds before an implementation of communitywide screening found that prevalence in 2010, after screening, was 0.8%, versus 0.04% in 2005, before screening, which suggests that early screening has contributed to increased prevalence of ASD (Nygren et al., 2012).

Over the past decade it has become clear that a number of social and cultural factors are associated with the likelihood of individuals receiving a clinical diagnosis of ASD in the community (Russell, Steer, & Golding, 2011). Social disadvantage, as related to parental education, income, socioeconomic status, and ethnic/minority status, are factors associated with underdiagnosis (Daniels & Mandell, 2014; Durkin et al., 2010; Shattuck et al., 2009), although these factors are not thought to influence the presentation of ASD. Previous reports had suggested a positive association between high social class or parental education and autism (Lotter, 1966; Wing, Yeates, Brierley, & Gould, 1976), although a more recent, large-scale epidemiological study failed to replicate an association, suggesting that prior results may have been confounded by the enhanced ability of educated upper-class families to obtain services (Fombonne, 2003).

EARLY MANIFESTATIONS AND COURSE

Kanner (1943) originally postulated that symptoms of ASD exist from birth, yet until the mid-1990s, it was uncommon for children to be diagnosed before age 4 or 5 (Howlin & Asgharian, 1999), so there was relatively little information on manifestations of autistic symptoms in the infant and toddler period. Since then, the impetus to improve outcomes via early interventions has motivated a series of retrospective and prospective studies of the development of autistic symptoms. This work has affirmed that ASD is a heterogeneous syndrome from its outset, with core symptoms that generally emerge by 12–24 months of age and are preceded by disruptions in nonsocial developmental domains.

Prospective infant sibling studies have elucidated early development in ASD by longitudinal tracking of infants at elevated familial risk for ASD via

an affected sibling. A major finding across these studies is that the development of language, nonverbal cognition, and early social communication in children display a marked deceleration in children with ASD. At 6 months of age, children who go on to have ASD have scores that do not significantly differ from those of typically developing infants at the group level in social function, nonverbal cognition, or preverbal language ability (Ozonoff et al., 2010). However, by 12 months, measurable differences emerge (Zwaigenbaum et al., 2005), with the first identifiable manifestations presenting as deficits in sensorimotor function and visual attention (Rogers, 2009). By 24 months, children with ASD score lower in most developmental domains (Estes et al., 2015; Landa & Garrett-Mayer, 2006), and a measurable decline in growth across skills domains is usually identified between the 12- and 24-month time points. The collective work from these studies, which include hundreds of children at high risk of ASD, provides strong evidence that early atypical developmental trajectories serve as risk indicators of ASD (Zwaigenbaum, Bauman, Stone, et al., 2015).

Social Communication Deficits: Infancy through Preschool

Among parents of children with ASD, roughly 30–40% have concerns about their child's development by the first year of life (De Giacomo & Fombonne, 1998) and the mean age of a child's initial presentation to a clinician is 18 months (Howlin & Asgharian, 1999). The frequent observation of developmental decline in high-risk infant sibling studies suggests that not all parents are sensitive to core symptoms of ASD or other developmental delays. Children with more severe delays are likely to be referred earlier (Daniels & Mandell, 2014) and firstborn children, whose parents likely have less experience witnessing early child development, are often diagnosed later (Zwaigenbaum, Bauman, Choueiri, et al., 2015). Clinicians should therefore be prepared to question parents directly about core features of ASD, as well as other delays and behavioral concerns in the infant and toddler period, which may be enriched in children with ASD but not specific to ASD.

The most common reason parents request evaluation is delayed speech and language development (De Giacomo & Fombonne, 1998; Stone, Coonrod, Turner, & Pozdol, 2004). Receptive and expressive aspects of language can be affected and may vary substantially among children with ASD, underscoring the syndrome's inherent heterogeneity. Receptive language delays, which involve difficulties with comprehension, tend to be greater and more predictive than expressive language delays in children with ASD. Concerns over expressive language may include a failure or delay in achieving verbal language milestones, such as babbling or spoken words, as well as atypical vocalizations, including grunting or echolalia. For children who present with more intact speech abilities, parents may note a reliance on scripted phrases or odd prosody.

It is less common for parents to present with specific concerns about

social development of children under the age of 3 years (Charman, 2002), although deficits in social communication can be elicited. In retrospective studies, parents have reported concerns for poor social awareness, poor social understanding, lack of shared enjoyment in interactions, and lack of interest in other children (Vostanis, Smith, Chung, & Corbett, 1994; Young, Brewer, & Pattison, 2003). Analyses of videotapes of infants prior to an ASD diagnosis demonstrated disruptions in early social behavior by 9 months of age, including looking at people infrequently, an absence of emotional expression, and poor social initiative (Adrien et al., 1993; Maestro et al., 2005). In their studies of videotapes from 12-month-olds, Osterling and Dawson (1994) observed that four features distinguished 91% of children with ASD from typically developing children: (1) lack of pointing, (2) lack of showing objects or things to others, (3) infrequently looking at faces, and (4) failure to respond to their own name being called. Other observations have included limited imitation, poor affect regulation, and reduced use of gestures (Maestro et al., 2002; Volkmar, Chawarska, & Klin, 2005; Yirmiya, Gamliel, Shaked, & Sigman, 2007). Retrospective studies also show that behaviors consistent with poor social orientation (e.g., responding to one's name) and social interest (e.g., looking at others) are specific in toddlers with ASD versus those with general developmental delay (Baranek, 1999; Osterling, Dawson, & Munson, 2002).

As children with ASD progress through the preschool period, they may improve in some of these infant social milestones. For example, more basic joint attention behaviors involving only eye contact have been shown to improve in children with ASD as they develop from a mental age of 18 months to 30 months (Mundy, Sigman, & Kasari, 1994). Nevertheless, preschool-aged children with ASD are often challenged by the increased demands of demonstrating appropriate social reciprocity and communication while interacting with a group, which may prompt parents to bring them to clinical attention after they enter a preschool setting.

Restricted, Repetitive Behaviors and Associated Behaviors

Restricted interests and repetitive behaviors have been observed in children with ASD during infancy and early toddlerhood (Rogers, 2009), although they generally become prominent later than do deficits in social communication skills (Cox et al., 1999; Moore & Goodson, 2003; Stone et al., 1999). These can be quite idiosyncratic and may involve extreme fixations, insistence on nonfunctional rituals, and distress with minor changes in their environment or schedule. Children may show odd attachments to toys, and their play may involve repeatedly lining things up rather than imaginative or narrative features. Some children display motor stereotypies, such as odd hand and finger mannerisms, or visual stereotypies, in which they repeatedly fixate on looking at objects out of the corner of their eyes, for example.

Sensory issues, now an aspect of the restricted, repetitive domain in DSM-5, are frequently reported in this age range. Common examples are

hypersensitivity to noise, tactile defensiveness, avoidance of certain food textures (often associated with a restricted diet), and hyposensitivity, such as a surprisingly high tolerance for pain. Other behavioral issues that are enriched but not specific to ASD include atypical reactivity, ranging from passivity to marked irritability. Sensory features and reactivity can exhibit both extremes in the same child. Difficulty sleeping is also common (Young et al., 2003). The motor domain is affected as well, and many parents report toe-walking (Hoshino et al., 1987; Tuchman & Rapin, 1997).

Clinical Presentation of Regression

A subset of parents also reports a history of regression, in which the child, who appeared to meet typical developmental milestones for the first 1–2 years of life, loses previously acquired skills. The majority of such cases occur between ages 13 and 18 months (Goldberg et al., 2003; Kurita, 1985; Werner & Dawson, 2005). Loss of language is the most common feature (Goldberg et al., 2003; Siperstein & Volkmar, 2004), although loss of social interest, interpersonal initiative, and basic social competencies, such as eye contact, have also been reported (Rogers & DiLalla, 1990). Other less commonly reported features include reduced variety and interaction in play, and loss of motor skills (Davidovitch, Glick, Holtzman, Tirosh, & Safir, 2000; Ozonoff, Williams, & Landa, 2005; Siperstein & Volkmar, 2004). Although regression was previously believed to be relatively rare, a review of six studies of clinical populations found a range of 22–50% in ASD (Fombonne & Chakrabarti, 2001), a figure subsequently supported by several studies drawn from the general population (Hansen et al., 2008; Taylor et al., 2002). Prognosis of regressive cases is unclear—regression has been associated with lower IQ (Rogers & DiLalla, 1990) but not consistently (Short & Schopler, 1988), and several reports have observed a mixed profile of strengths and weaknesses related to autistic severity, IQ, and adaptive function (Richler et al., 2006; Wiggins, Rice, & Baio, 2009).

Evidence for seizures as a contributor to regressive ASD is mixed, as co-occurrence of epilepsy is not universal (Hoshino et al., 1987; Kobayashi & Murata, 1998; Tuchman & Rapin, 1997). Nevertheless, the recognized link between regression and ASD has made any history of regression a "red flag" for referral (Filipek et al., 1999) and an indication for an electroencephalogram (EEG) to rule out a comorbid seizure disorder. Further evaluation in such cases is also important to distinguish possible ASD from neurodegenerative conditions that present with regression, such as Rett syndrome.

Developmental Timing of Diagnosis

An associated goal of characterizing earlier manifestations of ASD is ascertaining how to accurately identify those with a stable diagnosis at younger ages. Some work has suggested that ASD can be detected as early as the end

of the first year of life; however, on follow-up, a large percentage of these individuals are determined to have a different diagnosis (Landa, 2008). The largest body of evidence for diagnostic stability applies to children between ages 2 and 3 years. Multiple studies show good diagnostic stability (upwards of 80%) among 2-year-olds 1–7 years from the initial diagnosis (Eaves & Ho, 2004; Lord et al., 2006; Ozonoff et al., 2015; Stone et al., 1999; Turner, Stone, Pozdol, & Coonrod, 2006; van Daalen et al., 2009). Factors associated with less stability of an ASD diagnosis include age < 30 months at time of diagnosis (Sutera et al., 2007; Turner et al., 2006), lower severity of core symptoms (Rondeau et al., 2011), and the use of psychometric tools rather than clinical judgment to formulate a diagnosis (Charman & Baird, 2002; Lord et al., 2006; Stone et al., 1999).

One other consideration related to diagnostic stability is whether early evaluations for ASD in toddlers frequently miss diagnoses that can be identified later in the toddler period. This point was highlighted in a recent longitudinal study of infant siblings at risk of ASD by Ozonoff et al. (2015), who found that almost half the children in the sample diagnosed with ASD at 36 months (when evaluated using a clinical best estimate procedure) were not diagnosed when similarly assessed at 24 months. The authors concluded that longitudinal follow-up and repeated screening in the first years of life is critical for children with early social–communicative deficits, because in some cases a diagnosis of ASD may not be detected at younger ages.

Trajectories and Outcomes

During the preschool period, many children show greater variation in severity of core symptoms than what is observed at school age and beyond, which is characterized by considerable stability in ASD severity. Longitudinal analyses have generally shown that sizable proportions of individuals improve in core symptom severity, remain stable, or worsen, and some studies have reported a mean improvement in core symptoms over time (Charman et al., 2005; Pine, Luby, Abbacchi, & Constantino, 2006). Nevertheless, the field has been challenged to identify factors that are reliable and valid predictors of outcomes. In one study of children diagnosed at age 2, neither severity nor cognitive level predicted children who had lost an ASD diagnosis by age 4 (Sutera et al., 2007). In another study, the relationship between assessments at 2 years of age failed to predict level of function at 7 years of age, even when stratified by domains of social, communication, and restricted/repetitive behaviors, and social symptoms became increasingly variable over time (Charman et al., 2005). A recent study in preschoolers examined the trajectories of ASD symptom severity, adaptive function, and the relationship between the two (Szatmari et al., 2015). Interestingly, the correspondence between type of trajectory (improving, stable, declining) and symptom domain (core symptoms vs. adaptive function) was low, suggesting an added element of heterogeneity in the course of ASD.

Language outcomes have received a great deal of attention, both because language was previously a symptom domain of ASD and because it is one of the strongest predictors of overall outcome. Earlier language competence has been found to predict later language competence (Charman et al., 2005; Lord & Schopler, 1989; Sigman et al., 1999). A study by Hus, Pickles, Cook, Risi, and Lord (2007) encouragingly showed a greater variability of verbal language outcomes than expected, so that only 9.8% had no single words and 24% had no phrase speech, while 50% had normal word onset and 25% had normal onset of phrase speech. Work to investigate relationships between social developmental skills and language outcomes have repeatedly identified joint attention (Mundy, Sigman, & Kasari, 1990), imitation, and play abilities as positive predictors of language function in children with ASD (Toth, Munson, Meltzoff, & Dawson, 2006).

DIAGNOSTIC CRITERIA AND CHANGES WITH DSM-5

The diagnostic category "autistic disorder" was first introduced into the psychiatric classification system in the third edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III; American Psychiatric Association, 1980). The description, heavily influenced by Rutter (1978), broadly matched that of the more severe cases described by Kanner (1943), which were characterized by delay in language milestones and poor communication skills; intellectual disability (previously called "mental retardation"); social aloofness; motor stereotypes; and intense, narrow, and odd preoccupations. Over time, this narrower definition has been broadened to incorporate a spectrum of individuals impaired in core symptom domains to varying degrees of severity. The advent of DSM-5 has affirmed this conceptualization of autism as a spectrum, because two previous PDD diagnoses, Asperger syndrome and pervasive developmental disorder not otherwise specified, have been removed from DSM-5, and where appropriate, may be subsumed under the new ASD designation.

In addition, DSM-5 has incorporated scientific advances in its revisions related to ASD. Previously, autism had been viewed as a disorder having three symptom domains: reciprocal social behavior, language dysfunction, and excess of restricted interests and repetitive behavior. These three symptom domains have been collapsed into two domains—impaired social communication and restricted, repetitive interests and behaviors—based on evidence that the social and communicative impairments that are most specific to ASD (impairment in reciprocal social interaction and impairment in social/pragmatic aspects of communication) are closely interrelated, and their severity is highly correlated, not only within populations of clinically affected children (Gotham, Pickles, & Lord, 2012) but also in the general population (Constantino, 2011), with the caveat that results of factor analyses of ASD symptoms can be variable as a function of how they are ascertained.

Thus, the current diagnostic criteria include (A) persistent deficits in social communication and social interaction across multiple contexts; (B)

restricted, repetitive patterns of behavior, interests, or activities; (C) presence of symptoms in the early developmental period; (D) clinically significant impairment in social, occupational, or other important areas of current functioning caused by the symptoms; and (E) impairment that is not better explained by intellectual disability (intellectual developmental disorder) or global developmental delay (meaning that social communication should be below that expected for general developmental level). Furthermore, DSM-5 now calls for an improved understanding of both the individual's adaptive function and etiological factors. This has been integrated through the use of severity and clinical specifiers. The severity specifiers provide some characterization of adaptive function, which, like core symptom burden, is quantifiable. Clinical specifiers allow for listing of genetic or medical conditions that may be contributory, as well as clinical features that may help with future research into subcategories of ASD. An often overlooked aspect of the characterization of severity in ASD is that the core symptom burden (Criteria A and B) and impairment in social, occupational, or other important areas of adaptive functioning (Criterion D) are only partially correlated; there are many clinical situations in which core ASD symptom burden is pronounced but impairment in adaptive functioning is relatively mild, and vice versa. It can be well argued that most of the proven benefits of currently available interventions for autism are in the realm of adaptive functioning, not core symptoms counts (Lubetsky, Handen, & McGonigle, 2011; Charman & Gotham, 2013; Kanner, 1943). Improvements in adaptive functioning are achievable and critical for patients with ASD (Frith, 1991) but grossly underappreciated when measuring outcomes exclusively as a function of core symptom burden, as still often occurs in clinical trials. The hybrid severity index published in DSM-5 translates the effect of symptoms in each criterion domain (A and B) onto three broad categories of adaptive functioning, each of which is defined by descriptive scoring anchors that indicate the level of support that an affected individual requires.

Another noteworthy change in DSM-5 is that it is now deemed appropriate to diagnose ASD simultaneously with other psychiatric or developmental disorders (e.g., attention-deficit/hyperactivity disorder [ADHD]) when there is ample evidence for comorbidity, in view of overwhelming evidence that many known, inherited causes of ASD are genetically independent of the causes of other common neuropsychiatric disorders (Rutter, 1978), and it is therefore entirely possible for an individual to be affected by more than one neuropsychiatric condition. This also underscores the need to identify and treat comorbid disorders in children with ASDs. The change will help to ensure that, regardless of causes, all the needs of a developing child are recognized and addressed.

THE DIAGNOSTIC PROCESS

Implied, but not explicit in the diagnostic criteria themselves, are the elements of information gathering that are required to establish DSM-5 diagnostic Criteria A–E: (1) ascertainment of current symptomatology sufficient to meet

Criteria A, B, and D; (2) acquisition of a developmental history consistent with an ASD (Criterion C, provided by a primary caregiver of the child whenever possible); and (3) clinician confirmation.

One aspect of assessing symptomatology involves querying pathognomonic warning signs of ASD in the infant and toddler period. These include lack of protodeclarative pointing; lack of turn taking, reciprocal games (e.g., peekaboo); lack of symbolic interactive play (e.g., feeding a baby doll); avoidance of eye contact; failing to respond to one's name; stereotyped motor behaviors; and obsessive lining up of toys ("Learn the Signs. Act Early," 2015). Since the severity of current symptomatology can vary as a function of environmental context and demands, appraisal of symptoms also requires caregivers to provide accounts of an affected child's behavior across multiple environments: to report on social interests and evolving capacity for peer relationships; to provide information on day-to-day social communication (including use of verbal and nonverbal language and communication, imagination and play); to describe sensory responses and the frequency of repetitive or stereotypical behaviors of ASD, including behavioral rigidity; and to detail self-help skills and propensity for moodiness, tantrums and outbursts.

Similarly, clinician confirmation relies on a diversity of prompts to elicit a child's highest capacity for social communication, and to introduce enough sensory arousal to elicit stereotyped responses if they are not immediately evident. Depending on the age of the child, this interaction can be a play-based assessment with toys commonly used by children within the local community or a more conversational interaction in which the child is asked about his or her life at home and at school, friendships, and daily interactions with peers. Having made direct observations of the child and gathered adequate information to satisfy criteria A, B, and D, the clinician must determine that the clinical-level impairment in adaptive functioning is largely attributable to ASD and not to an alternative psychiatric or developmental, or neurological disorder. For example, it is important for clinicians to rule out specific, potentially treatable causes of autistic syndromes, particularly in patients who are manifesting signs that may be caused or exacerbated by such conditions. These include primarily epilepsies (Box 8.1) and metabolic disorders (see Table 3.1 in Lubetsky et al., 2011). Any suspicion of these would warrant consultation and referral to a neurologist. For more detailed information on assessment algorithms, we refer the reader to previously published sources (McConachie et al., 2015; Zwaigenbaum, Bauman, Choueiri, et al., 2015); a resource for assisting clinicians in the identification of treatable causes of cognitive delay in early childhood can be found at *http://treatable-id.net*.

What becomes immediately evident in the diagnostic process, especially for milder ASD syndromes, is that fulfillment of DSM-5 Criteria A, B, and D is, by definition, exquisitely sensitive to the notion of clinical threshold. There is an apparent tension between expert clinician judgment about where these thresholds should lie and the fundamental nature of the features described by Criteria A, B, and D (their respective distributions, interrelations, and

BOX 8.1. Behaviors of Concern for Epilepsy in Young Children

INFANTILE SPASMS

These specific types of seizures are sudden, uncontrolled movements of a child's neck, body, arms, and legs. They last only for a few seconds and often occur in clusters lasting several minutes, during which more than 100 can occur. Spasms are most common during the early morning or when a child wakes up from a nap. Below are some common features:

- Repetitive forward head nodding or bobbing
- Bowing from the waist when sitting
- Drawing up of knees when lying down
- Extending or stiffening of the neck, trunk, arms, and legs
- Crossing arms across body as if self-hugging
- Thrusting arms to the side, elbows bent

FOCAL SEIZURES

Simple Focal Seizures

Symptoms vary depending upon which area of the brain is involved. More commonly, a child's muscles are affected. The seizure activity is limited to an isolated muscle group, such as fingers or to larger muscles in the arms and legs. Consciousness is not lost in this type of seizure. The child may also experience sweating or nausea, or become pale.

Complex Focal Seizures

This seizure usually lasts 1 to 2 minutes. Consciousness is usually lost during these seizures, so that a child stops being aware of what's going on around him or her. The child may look awake but have a variety of behaviors, ranging from gagging, lip smacking, running, screaming, crying, and/or laughing. When the child regains consciousness, he or she may complain of being tired or sleepy.

GENERALIZED SEIZURES

Absence Seizures (Also Called Petit Mal Seizures)

These seizures are characterized by a brief altered state of consciousness and staring episodes. The mouth or face may move or the eyes may blink. The seizure usually lasts no longer than 30 seconds, and the child may not recall what just occurred. These seizures may occur several times a day.

(*continued*)

BOX 8.1. (*continued*)

Atonic Seiuzures (Also Called Drop Attacks)

With atonic seizures, there is a sudden loss of muscle tone and the child may fall from a standing position or suddenly drop his or her head. During the seizure, the child is limp and unresponsive.

Generalized Tonic–Clonic Seizures (Also Called Grand Mal Seizures)

The classic form of this kind of seizure is characterized by five distinct phases. The body, arms, and legs will flex (contract), extend (straighten out), tremor (shake), a clonic period (contraction and relaxation of the muscles), followed by the postictal period. Not all of these phases may be seen with every one of this type of seizure. During the postictal period, the child may be sleepy, have problems with vision or speech, and may have a bad headache, fatigue, or body aches.

Myoclonic Seizures

This type of seizure refers to quick movements or sudden jerking of a group of muscles. These seizures tend to occur in clusters, meaning that they may occur several times a day, or for several days in a row.

Note. Based on *www.hopkinsmedicine.org/healthlibrary/conditions/pediatrics/seizures_and_epilepsy_in_children_90,P02621* and *www.actharis.com/understand-infantile-spasms/know-the-causes-and-symptoms.html.*

biological causes) that raises continuously evolving questions about how the clinical thresholds for these criteria should be established for the purpose of diagnosis. Should they represent percentile cutoffs of the normal distribution (as dominates the diagnosis of intellectual disability)? Should absolute symptom burden or level of impairment of adaptive functioning dominate parameterization of the clinical threshold? In traditional ASD research, emphasis has unequivocally been on the former, although the introduction of severity specifiers in DSM-5 now encourages evaluation of adaptive functioning in the diagnostic process for ASD.

DIFFERENTIAL DIAGNOSIS

The conditions listed below are often associated with impairments in social skills, communication, or an excess of restricted, repetitive behaviors. However, in these conditions, such symptoms do not represent a core disruption in social development, but occur secondarily, in the context of the other disorder, which affects the choice of intervention strategy. A careful developmental history is paramount to establish whether these symptoms are attributable to

ASD or another disorder, or whether there is a psychiatric comorbidity, which has been found to occur in up to 72% of children with ASD (Leyfer et al., 2006).

Intellectual Disability

Intellectual disability (ID) is associated with impairments in "adaptive" social function, the skill with which the child carries out social interactions in everyday life (American Psychiatric Association, 2013). Children with ID (likely described as having developmental delay in the preschool period) exhibit language delays that constrain their communication. They may also display elevated restricted, repetitive behaviors relative to typically developing children. Unlike in ASD, however, children with ID show interest in social engagement (Ventola et al., 2007), and as a result, social overtures should occur at a level consistent with their cognitive development. When social disturbances exceed what would be expected for cognitive delays, a comorbid diagnosis of ASD is more likely to apply.

Two specific disorders featuring ID and social dysfunction are Rett syndrome and fragile X syndrome. Rett syndrome, like ASD, was previously categorized as a pervasive developmental disorder (American Psychiatric Association, 2000). It is distinguished from ASD by affecting females and displaying a consistent course of typical development for the first 2 years of life, followed by a decline in head circumference growth and behavioral abilities in cognitive, motor, and social domains. Children with Rett syndrome develop distinctive stereotyped, repetitive hand motions. Fragile X syndrome is the genetic condition most strongly associated with ASD. Individuals with fragile X syndrome are usually male and often have a high degree of anxiety, whether or not they meet criteria for ASD. For those individuals with Rett or fragile X syndrome who do meet criteria for ASD, a specifier indicating that ASD is related to a medical condition should be included in the ASD diagnosis.

Language Disorders

Many early referrals for ASD in fact have a language disorder, which is more common than ASD. Like children with ASD, children with language disorder may have difficulties communicating effectively, although this difficulty stems from issues with structural language (e.g., vocabulary and grammar) rather than deficiencies in social interest. Some children with language disorders can appear socially awkward, but again, their interest in social interaction and relationships would be expected to be intact, in contrast to that of a child with ASD. One of the more nuanced distinctions, however, has come with the new diagnosis of "social communication disorder" in DSM-5. This diagnosis resembles ASD in that children struggle with appropriate language use (i.e., language pragmatics) based on their ability to understand and follow social rules related to verbal and nonverbal communication, but unlike children with ASD, they lack restricted interests or repetitive behaviors.

Attention-Deficit/Hyperactivity Disorder

Children with ADHD can show elevated levels of autistic traits and often have difficulty maintaining positive social interactions. Conversely, many children with ASD can appear physically restless, distracted, impulsive, and reactive. In cases in which a child's restlessness appears largely linked to discomfort in social situations or sensory overstimulation, the inattention appears primarily during social interactions, and reactivity is linked to rigidity or sensory issues, a diagnosis of ASD should be considered.

Anxiety Disorders

Anxiety disorders are extremely common, and children with anxiety disorders may frequently demonstrate impaired social skills and communication. Upon deeper examination, these are primarily related to inhibition and fearfulness (e.g., as in the case of selective mutism) rather than a core deficit in social interest, awareness, or understanding. Furthermore, for children with obsessions and compulsions, their fixations and ritualized, compulsive behaviors are often ego-dystonic rather than self-stimulating, as is often the case with ASD.

Disruptive Behavior Disorders

Children with disruptive behavior disorders often appear uncooperative, defiant, and inclined to annoy others. Perceived noncompliance in children with ASD likely stems from core symptoms related to lack of social awareness, difficulty tolerating change or specific demands, or sensory defensiveness rather than purposeful defiance. Comorbid diagnoses in this category should therefore be conservatively applied.

PROGRESS IN THE MEASUREMENT OF AUTISTIC TRAITS

Standardized Measures of Symptom Burden

A range of screening and diagnostic instruments for ASD has been developed over the past two decades. We refer the reader to two very recent open-access reports which have synthesized the sizable literature on early diagnosis of ASD (Zwaigenbaum, Bauman, Choueiri, et al., 2015) and characterization of progress and outcomes in preschool children with ASD (McConachie et al., 2015). From the latter, we reproduce two tables here that summarize available methods used to characterize symptom severity and level of intellectual functioning (see Tables 8.1 and 8.2).

We note that some of the more time-intensive instruments that have been relied upon in traditional approaches to diagnostic assessment—and that have been increasingly adopted in the United States as *prerequisites* for

TABLE 8.1. Summary of Quality: Autism Symptom Severity

		Reliability				Hypothesis testing			Responsiveness	
Tool (number of papers)	Internal consistency	Test–retest	Interrater	Content validity	Structural validity	Convergent/ divergent validity	Known groups	Criterion validity	Stability	Change
Autism Behavior Checklist (3)	++		?		+					
Autism Diagnostic Interview—Revised (12)	+++		++	+++	+/–	– –	++	++	++	
Autism Diagnostic Observation Schedule (7)	?	?	+	+	+++			++	++	
Autism Diagnostic Observation Schedule—Toddler Module (1)	+/–	+/–	?	+						
Autism Diagnostic Observation Schedule—Calibrated Severity Score (3)							+++		+	
Autism Observation Scale for Infants (2)		?	?				++			
Baby and Infant Screen for Children with Autism Traits—Part 1 (3)	++				– –	++	++			
Behavioral Summarized Evaluation (1990) and Behavioral Summarized Evaluation—Revised (1997) (4)	?		+	+++	+/–	+	+	?		
Infant Behavioral Summarized Evaluation (1)			+		?					

(*continued*)

TABLE 8.1. (*continued*)

		Reliability				Hypothesis testing			Responsiveness	
Tool (number of papers)	Internal consistency	Test–retest	Interrater	Content validity	Structural validity	Convergent/ divergent validity	Known groups	Criterion validity	Stability	Change
Childhood Autism Rating Scale (10)	+++	+++	+++		+/–	– –				
Gilliam Autism Rating Scale (3)	+++		– –		– – –		–			
Modified Checklist for Autism in Toddlers (3)	?	?	?					+		
Parent Observation of Early Markers Scale (1)	++	?				–				
Pervasive Developmental Disorders Rating Scale (2)	++	+			?					
Real Life Rating Scale (2)	?		?							
Social Communication Questionnaire (3)	++				++			++	+	
Social Responsiveness Scale (5)	+++	+/–	+/–		– – –	++	+	– –		

Note. +++ or – – –, strong evidence; ++ or – –, moderate evidence; + or –, limited evidence; ?, unknown, owing to poor methodological quality; blank cell, no evidence available. From McConachie et al. (2015). Copyright © Queen's Printer and Controller of HMSO 2015. Reprinted by permission.

TABLE 8.2. Summary of Quality: Cognitive Ability

	Reliability					Hypothesis testing			Responsiveness	
Tool (number of papers)	Internal consistency	Test–retest	Interrater	Content validity	Structural validity	Convergent/ divergent validity	Known groups	Criterion validity	Stability	Change
Leiter International Performance Scale—Revised (3)										
Mullen Scales of Early Learning (2)							−−	++		
Mullen Scales of Early Learning—Early Learning Composite (1)							++			
Stanford–Binet Intelligence Scales—Fifth Edition (1)						+	−			
Wechsler Preschool and Primary Scale of Intelligence—Revised (1)										−

Note. +++ or − − −, strong evidence; ++ or − −, moderate evidence; + or −, limited evidence; ?, unknown, owing to poor methodological quality; blank cell, no evidence available. From McConachie et al. (2015). Copyright © Queen's Printer and Controller of HMSO 2015. Reprinted by permission.

both service eligibility and research participation—are expensive and difficult to acquire consistently in public health settings. Some of the more rapid methodologies represented in the current list of available assessment tools, as they are increasingly validated and refined, are constituting components of cost-effective strategies for the assessment of children affected by ASD, allowing a shift in available resources toward treatment and the acquisition of repeated measures data, which is vital to the evaluation of response to intervention. When combined with rapidly obtainable information on developmental history and current symptomatology in daily social contexts, standardized observational ratings by clinicians—*without* the need for extensive rater training—show tremendous promise for the diagnostic confirmation of ASD (Constantino et al., 2012).

Although there is, as expected, overlap in the concepts and the content of ASD ratings scales and diagnostic instruments, they differ in the aspect of the diagnostic process to which they apply (i.e., developmental history vs. current symptom ascertainment vs. clinician confirmation), the populations for whom they are standardized, and the degree to which they are sensitive measures of subclinical variation in ASD traits. They also vary in terms of the need for trained raters, the time needed to train raters or to complete assessments, and the cost and feasibility of application in clinical settings. Among the most notable limitations is the degree to which the accuracy of many screening and diagnostic instruments has been validated in individuals with ASD with intellectual disability.

Quantitative Approaches to the Measurement of Autistic Traits

When standardized methods for quantitative assessment of ASD symptoms and traits have been applied to the general population, the unequivocal result from a host of studies, implementing numerous measurement instruments, is that the characteristic traits and features that characterize autism are continuously—not bimodally—distributed in nature (Constantino, 2009; Kim & Leventhal, 2015; Ronald et al., 2014; Yuen et al., 2015).

Recently we reported the results of an attempt to examine the traits and symptoms of ASD in toddlers—quantitatively characterized using a video-referenced rating system (Marrus et al., 2015). This instrument asks caregivers to rate their child's social behavior against a typically developing child observed in a video clip, with the goal of improving on the ability of current ASD screening tools to (1) measure features of autistic syndromes typically first appreciable in clinical settings and (2) track developmental trajectories and monitor responses to interventions. In an epidemiological sample of toddler twins ages 18–24 months, we observed that, as has been shown at older ages, levels of reciprocal traits appear heritable, correlate with level of ASD risk, and display a continuous unimodal distribution (Figure 8.1). This observation implies that there is an arbitrary nature to diagnostic cutoffs in ASD

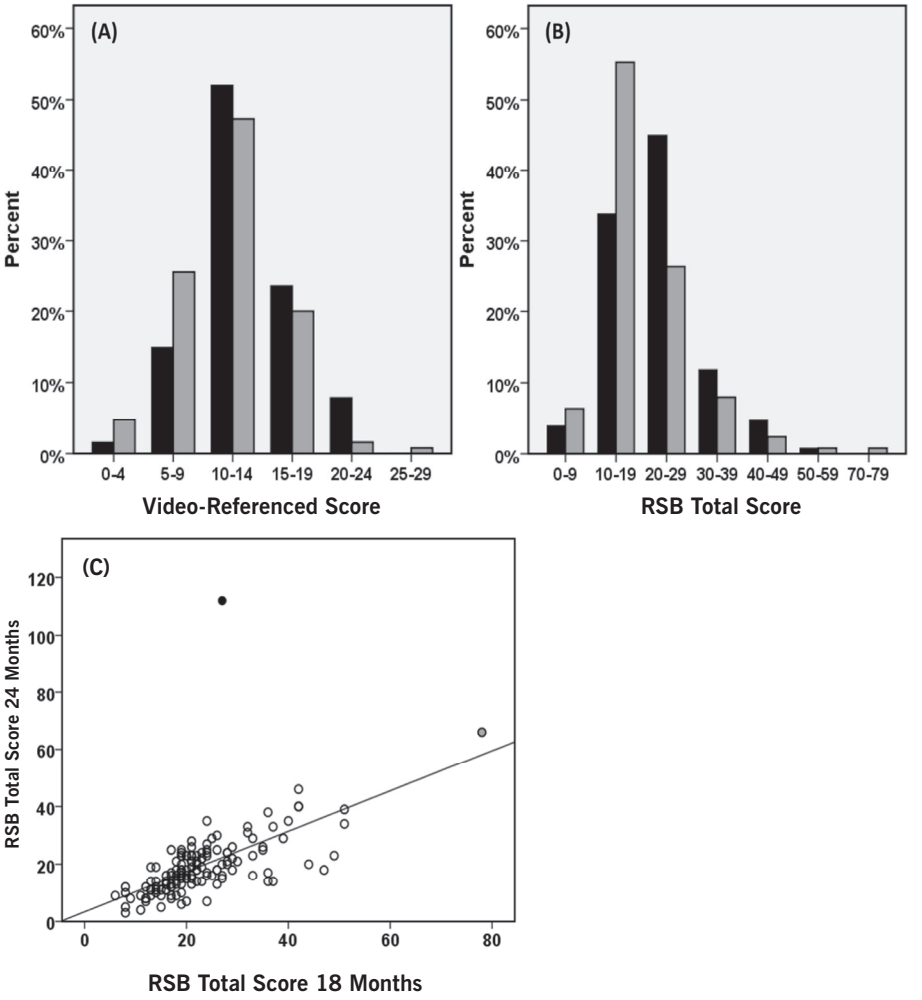

FIGURE 8.1. Psychometric properties of the video-referenced Rating Scale of Reciprocal Social Behavior (vrRSB). Panels A and B illustrate 18-month scores on the vrRSB. Male and female scores are indicated with black and gray bars, respectively. Scores on video-referenced items are shown in Panel A and for the total instrument in Panel B (total = video-referenced + non-video-referenced items). Distributions are continuous and higher scores indicate decreased levels of reciprocal social behavior. As in older populations, male toddlers show a rightward shift, suggesting lower levels of RSB. In Panel C, the intraclass correlation coefficient of .704 ($p < .001$) is consistent with excellent test–retest reliability between 18 and 24 months. The black dot indicates a child whose parents reported regression between 18 and 24 months, by which time a community diagnosis of ASD had been established.

and points to the need for methods of the type that have been applied to other quantitative human traits—such as height, weight, intelligence, blood pressure—to derive standardized, percentile-based guidelines for clinical diagnosis. Remarkably, the characteristic traits and symptoms of the autistic syndrome (deficits in reciprocal social behavior, impairment in social communication, repetitive behavior, and restriction in range of interests) are as highly interrelated in the general population as they are (by definition) in individuals with clinical ASD syndromes. Such homologous factor structures substantiate the use of unitary scores (akin to IQ for intelligence) as valid indices of symptom burden in both clinical and nonclinical populations (Constantino et al., 2013), even though the overlap in biological causation of the respective symptom domains is not fully understood.

At present, whether subprofiles of the autistic syndrome—featuring, more or less, involvement of one or another of the respective symptom domains—will reliably map to independent sets of biological causes remains unclear (De Rubeis et al., 2014). Furthermore, when standardized quantitative methods are implemented in the study of families affected by ASD, subclinical autistic symptoms and traits are observed among first-degree relatives with a frequency and order of magnitude higher than that observed in the general population (Ramu et al., 2013; State & Geschwind, 2015). Recently, in very large genetic–epidemiological studies, it has been confirmed that the genetic susceptibilities to these subclinical syndromes exhibit near-complete overlap with genetic underpinnings of the clinical-level syndromes (Shetreat-Klein, Shinnar, & Rapin, 2014), strongly suggesting that the continuous distributions observed in nature relate to quantitative accumulation of causal susceptibility. A more detailed review of discrete subpopulations that partly contribute to the continuum observed in nature has been published previously (Ronald et al., 2014). Thus, although the diagnostic criteria for ASD do not yet consider percentile rank in the population distribution (as do diagnostic criteria for anorexia nervosa, hypertension, intellectual disability, and short stature), an increasingly compelling case can be made for parameterizing diagnostic thresholds in this manner.

Moreover, in the same way that height influences weight, the neurodevelopmental characteristics of intelligence, attention, structural language capacity, emotion regulation, and executive function can influence social communication, such that specification of the role of autistic symptomatology in an individual patient will ultimately require established maps of the predictable relations between the variables (analogous to the height vs. weight norms for males and females used in pediatric practice) to accurately ascertain the relative contribution of ASD symptomatology to a given neurodevelopmental syndrome (Jones, Gliga, Bedford, Charman, & Johnson, 2014). This is becoming especially relevant as we understand more fully the biological influence (effect of inheritance) on each (separable) axis of human development, and we recognize that even rare monogenic syndromes commonly have adverse influences on multiple domains of development (e.g., effects of 16p11.2 rearrangements

on intelligence, social responsiveness, and weight; Gotham et al., 2012), each influenced by the mutation in a manner that represents a predictable shift against a (biparental) genetic and environmental background for that trait. In this way, rare syndromes can be more deeply understood, not simply by the variable and idiosyncratic array of deficits with which they are associated, but by how they influence such traits in the setting of the specific genetic and environmental background of an individual.

CAUSATION AND AN IMPENDING REVOLUTION IN ASD DIAGNOSIS

The past decade has witnessed an explosion in scientific discovery of the causes and biology of autism. Twin and family studies involving tens of thousands of individuals in ASD-affected families have overwhelmingly established the important role of genetic factors in the causation of most autistic syndromes (Green, Charman, Pickles, Wan, Elsabbagh, et al., 2015; Lord, 1995; Rogers et al., 2014), and growing genetic evidence has implicated genes involved in synaptic development and plasticity (De Rubeis et al., 2014). Emerging work in neuroimaging and EEG studies has also identified brain differences associated with ASD during early childhood, including (1) structural alterations in regions important for socioemotional processing and regulation (e.g., amygdala; Mosconi et al., 2009; Schumann, Barnes, Lord, & Courchesne, 2009); (2) altered developmental trajectories of the integrity of multiple white-matter tracts (Wolff et al., 2012); and (3) altered functional connectivity (Boersma et al., 2013). In aggregate, this work has implicated developmental disruptions at multiple levels of neural architecture, from cellular connections to interregional neurocircuitry, in the emergence of ASD. Although neither a laboratory test nor a neural signature to date can reliably establish the presence of a nonsyndromic ASD, a rapidly increasing proportion of all cases—approaching the majority—can be attributed to the influence of deleterious molecular genetic variants or combinations of variants. It is expected that understanding these aspects of the genetics of autism will play a major part in revolutionizing diagnosis. We refer the reader to Constantino and Charman (2016) for an extensive recent review of the implications of advances in genetics on the diagnosis of ASD.

Resolution of many autistic syndromes with respect to the relative contribution of specific genetic variants also continues to illuminate understanding of the biology of autism comorbidities, such as ADHD, motor coordination impairment (Charman & Baird, 2002; Lord et al., 2006; Turner et al., 2006), epilepsy, intellectual disability, anxiety, and the psychopathologies. Although none of these symptom clusters is specific to ASD, some mutations (e.g., those associated with fragile X syndrome (*FMR1*), neurofibromatosis type 1 (*NF1*), tuberous sclerosis, and a host of newly discovered variants) have been associated with predictable profiles of comorbidity (whenever ASD arises) and

therefore blur the distinction between core symptoms and associated symptoms, at least in the setting of these monogenic syndromes (Fountain, Winter, & Bearman, 2012).

In summary, advances in understanding the causes of autism—its genetic and population structure—suggest that diagnosis will ultimately benefit from further movement toward standardized quantitative characterization of the defining features of ASD, conducted simultaneously with (and controlling for) multiaxial characterization of those aspects of human development that influence the manifestation of autistic symptoms and impairments, and from the inclusion of genotype in taxonomic classification. For some putative causes of ASD, we are still at an early stage in the conversion from statistical association in large genetic studies to knowledge of the specific impact of a deleterious variant in an individual patient.

Efforts to advance earlier diagnosis have also revealed neurocognitive signatures of early ASD risk that may yield a first generation of diagnostic biomarkers that are shared by many or most autistic syndromes. Studies of infants at familial risk of ASD have utilized novel technologies, including eye tracking and EEG/event-related potential (ERP) methods, to study the infant neurocognitive predictors of later ASD diagnosis (Dawson et al., 2010). A number of neurocognitive biomarkers have been identified in the first year of life. These include differences in social response, such as a decline in eye fixation when viewing faces between ages 2 and 6 months (Jones & Klin, 2013) reduced social orienting (Chawarska, Macari, & Shic, 2013) and a reduced neural response to dynamic gaze shifts from 6 months of age (Elsabbagh, Mercure, et al., 2012). However, differences in nonsocial neurocognitive processes have also been associated with later ASD, including shorter fixation duration at 7 months of age (Wass et al., 2015) and a decline in attentional disengagement ability between 7 and 14 months (Elsabbagh et al., 2013). Although no integrative theoretical account has achieved widespread acceptance, several models of emergent neurodevelopmental atypicality have been proposed (Gliga, Jones, Bedford, Charman, & Johnson, 2014; Klin, Shultz, & Jones, 2015). The clinical field awaits the outcome of the translational work (which has now begun) before such technologies can be used in a reliable way to augment behavioral assessment of individual infants and toddlers to aid early diagnosis in the future.

GUIDANCE FOR FAMILIES AFFECTED BY ASD

Mental health care providers play a critical role in helping families obtain comprehensive, evidence-based treatment (Box 8.2). During the preschool period, a stage of heightened neural plasticity, the provider's first responsibility is to ensure that the child receives intensive early intervention and developmental therapies. These interventions should prioritize language and communication, because the capacity to communicate is the most important predictor

BOX 8.2. Family Guidance: Components of a Comprehensive Approach to the Support of a Preschool Child with ASD

INTERVENTION PLANNING

- Obtain clinical diagnosis of ASD by a pediatrician, developmental pediatrician, child neurologist, or a qualified child psychiatrist (i.e., with experience/expertise in early childhood psychopathology); a critical aspect of diagnosis is to rule out the presence of treatable neurological syndromes (epilepsy, metabolic disorder), hearing impairment, or sensory impairment.
- Ascertain and define treatment approach to any "comorbid" developmental or neuropsychiatric disorder (ADHD, disruptive mood dysregulation disorder).
- Institute developmental therapies—to include speech and language therapy and early intensive behavioral intervention, as indicated.
- Implement pharmacotherapy, when irritability, aggression, emotion dysregulation, hyperactivity, or impulsivity severely compromise child's ability to respond to developmental therapy. Examples include:

  Stimulants: dextroamphetamine is FDA approved for preschool ages.
  Alpha agonists: clonidine, guanfacine.
  Atypical neuroleptics: risperidone and aripiprazole are FDA approved for irritability and aggression.

EARLY CHILDHOOD EDUCATION

- Ensure the appropriate level of structure/support, optimizing intervention in "least restrictive" setting.
- Prioritize above all the acquisition of communicative (language) and social competencies.
- Incorporate applied behavior analysis-based methods when appropriate.

PARENT EDUCATION

- Promote understanding of autism as a heterogeneous neurodevelopmental condition benefitting from individualized, multidisciplinary treatment.
- Encourage parent training, including specific strategies for children with developmental challenges.
- Highlight prospects for optimizing adaptive function at each successive developmental stage and opportunities for parents to serve as advocates for their child's needs.

FAMILY SUPPORT

- Address the needs and burdens encountered by siblings of children with developmental disability.
- Recognize indications for targeted implementation of family/couple therapy.
- Promote awareness of state and federal laws that substantiate effective legal advocacy for children with ASD.

of adaptive functioning. Fostering socioemotional development, including self-regulation and social reciprocity, is an additional pillar of a well-rounded program.

Children with ASD often demonstrate associated challenging behaviors, or comorbidities, both psychiatric and medical, which, in the context of ASD can profoundly impact quality of life and adaptive function. Evaluations by physicians with expertise in neurodevelopmental conditions and psychopathology is important to rule out treatable neurological syndromes and diagnose and treat comorbidities. Use of pharmacotherapy for disruptive behaviors and psychiatric comorbidities should be preceded by a careful assessment of risks and benefits, the latter of which may include safety or improving the child's participation in behavioral interventions. Providers also guide families to obtain the indicated multidisciplinary, community-based resources, including applied behavior analysis, speech and language therapy, occupational therapy, and physical therapy. Early childhood special education often serves as a major platform for delivery of these and other interventions via an individualized educational plan.

On an interpersonal level, mental health care providers help empower families as they confront the challenges of raising a child with ASD. Educating families about strategies for managing challenging behaviors in the home, critical evaluation of alternative treatments, or situations in which to obtain legal advocacy promote family-centered care. When families are in need of psychosocial supports, physicians can reassure them that their own well-being, which may be overlooked, is a priority of the treatment plan.

Establishing a collaborative, consultative relationship with families is key for clinicians to effectively guide families in accessing appropriate resources and implementing comprehensive interventions. Within this supportive context, clinician guidance is translated into an individualized treatment program that is tailored to a child's specific strengths and weaknesses, maximally capitalizing on a critical developmental window for improving outcomes in ASD.

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9

Attachment Disorders

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Attachment theory is an important way to conceptualize how infants and young children begin to understand and develop relationships. Early problems developing attachment to a caregiver may cause later problems with developing and sustaining healthy relationships. When the development of attachments is impeded by insufficient caregiving, children may develop an attachment disorder. Although attachment disordered behavior has been described in the literature since the 1950s, there was almost no research on the subject until the mid-1990s. Even today, some confusion remains regarding the terminology, focus, breadth, and significance of attachment disordered behavior.

In this chapter, we review the developmental significance of attachment, with special attention to the preschool period. We also discuss the assessment and classification of patterns of attachment. Next, we review the clinical presentation of two attachment disorders, reactive attachment disorder (RAD) and disinhibited social engagement disorder (DSED). We discuss what is known about the risk factors, neurobiology, prevalence, course, and comorbidities of each. Finally, we offer guidelines for the assessment and treatment of preschool children with these disorders.

THE DEVELOPMENT OF ATTACHMENT

"Attachment" is an innate behavioral system that motivates young children to seek comfort, support, nurturance, and protection from discriminated attachment figures. From an evolutionary perspective, this helps ensure survival of

offspring by promoting mutual proximity of infants and caregivers, thereby protecting children from danger. To ensure proximity-seeking behavior, infants must reference and respond to their caregivers' signals and signal their caregivers. The communication triggered by the attachment system also helps infants learn to regulate their developing emotional states.

Children are not born attached to their caregivers; rather, they become attached to specific caregivers through a gradual, unfolding process. At birth, infants have a limited ability to distinguish between different people, and they display behavioral signaling indiscriminately. Infants learn through their experiences to develop a preference for a caregiver who meets their physical and emotional needs (Ainsworth, 1967; Bowlby, 1982). Around age 2–3 months, infants begin to show different behavioral interactions with their primary caregiver(s) in comparison to other adults. They also show more social communication, for example, smiling in response to attention from a parent. Around 7–9 months, infants develop the capacity to form a preferred attachment to a caregiver. The infant begins to demonstrate attachment to its mother (most typically), with a striking decline in social engagement with others. Protests at the mother's departure also develop at this time. The infant tries to maintain proximity to the caregiver by both physical action and social signals (Bowlby, 1982).

As infants continue to develop, the onset of crawling and walking allows for new attachment behaviors to be displayed. Infants venture out into the world, using the attachment figure as a "secure base" from which to explore. In times of danger, infants return to the attachment figure, using her as a "safe haven" (Ainsworth, 1967). Later, elaboration of the infant's cognitive skills and memory allows for the development of a rudimentary "internal working model." The working model is a psychological construct to understand the relationship between the world, the self, and others. Finally, in the later toddler and preschool years, further cognitive, communicative, and emotional development allows for the formation of a "goal-corrected partnership." This is a more complex and rich relationship with the caregiver in which children begin to appreciate the needs of others and also learn to negotiate to get their own needs met.

The attachment system is complemented by other important behavioral systems, including an exploratory system, a fear/wariness system, and a sociable/affiliative system. The "exploratory system," supported by developing motor skills, allows the infant to learn through interaction with the physical and social environment. The attachment and exploratory systems act in tandem. When the child feels comfortable with a caregiver's availability, attachment is relatively deactivated and the child is motivated to explore the immediate environment. If the attachment system is activated by fear or distress, exploration is then deactivated, and the child seeks proximity to the caregiver. The "fear/wariness system" coordinates fearful responses to strangers and new situations. The "sociable/affiliative system," which is sometimes confused with the attachment system, motivates children to go out and engage

socially with others. The behaviors associated with these systems are coordinated in such a manner that they inhibit or potentiate one another.

ASSESSMENT AND CLASSIFICATION OF ATTACHMENT

The way a child and a caregiver develop an attachment has important implications for how the child interacts with the world, organizes emotions, and maintains relationships. Each attachment relationship exists on a continuum ranging adaptive to maladaptive. The Strange Situation Procedure (SSP; Ainsworth, Blehar, Waters, & Wall, 1978) is a laboratory procedure that is designed to evaluate the parent–child attachment relationship. This procedure was originally used for children between 12 and 20 months of age. The SSP consists of eight discrete episodes designed to increasingly activate the infant's attachment system through a series of brief, controlled separations and reunions with an attachment figure and a stranger. Using this procedure, attachments may be classified as secure, insecure-avoidant, insecure-resistant, or disorganized. (Figure 9.1 shows other attachment classification systems).

A "securely attached" infant demonstrates a comfortable balance between attachment and exploratory behaviors. Securely attached infants use their caregivers as a secure base from which to explore and a safe haven to return to in times of danger. Infants classified as "insecure-avoidant" seem to turn their attention away from their own distress and focus instead on exploration. Even though physiologically aroused by distress, they effectively suppress their need for comfort and have attachment systems that remain relatively deactivated. Infants classified as "insecure–resistant," on the other hand, activate their attachment systems in response to separation but have difficulty deactivating it during reunion; that is, they are typically distressed by the caregiver's departure but fail to settle down when the caregiver returns, often greeting the caregiver's return with a mixture of contact seeking and

	Secure strategies	Insecure strategies			
Infants 12–20 months (Ainsworth et al., 1978)	Secure	Avoidant	Resistant	Disorganized	Unclassifiable
Preschoolers 24–48 months (Cassidy & Marvin, 1987)	Secure	Avoidant	Dependent	Controlling/ disorganized	Insecure/other
	Organized strategies		Not organized strategies		

FIGURE 9.1. Classifications of attachment in toddlers and preschoolers.

rejection (showing a resistance to comfort or contact). Infants with "disorganized" attachment demonstrate atypical reunion behaviors, such as dissociative or disoriented episodes, as well as poorly integrated mixtures of secure, avoidant, and ambivalent behaviors (Main & Solomon, 1988).

The SSP classification patterns are associated with the parental care the child receives. Securely attached infants typically have caregivers who are emotionally responsive to their distress and bids for comfort. Infants with insecure–avoidant attachments typically have caregivers who are uncomfortable responding effectively to emotional needs; because the parent is uncomfortable, he or she tacitly discourages the child from seeking comfort when distressed. For example, a caregiver might frequently refocus a distressed child on exploration instead of helping organize the child's feelings and providing comfort. The child then learns to avoid seeking out the caregiver. Caregivers of insecure–resistant infants are typically inconsistent in their responsiveness to the child. In this situation, infants learn to activate the attachment system continuously in order to keep the caregiver available to meet their physical and emotional needs. With the child's attachment system always activated, these dyads tend to have a difficult time with separations (and reunions), the caregiver may appear anxious or needy, and he or she often does not support the child's exploration. Disorganized attachments are associated with high-risk environments and are often the sequelae of threatening, frightening, or dissociated caregiving (Main & Hesse, 1990). In disorganized attachment, the attachment figure is both the *solution to* and the *source of* the attachment alarm. Fear of the parent activates the attachment system and the drive for proximity; however, as proximity increases, the fear of the parent also increases. This leads to what ethologists term "conflict behavior," which the child manifests as disorganized attachment behaviors. There is increasing evidence that disorganized attachment confers a significant risk for psychopathology (Green & Goldwyn, 2002; Zeanah, Berlin, & Boris, 2011). Conversely, secure attachment is a protective factor, especially within high-risk samples (see McGoron et al., 2012).

An assessment of attachment, such as the SSP, takes into consideration both the child's use of a caregiver and the caregiver's response to the child. Because the attachment strategy is constructed interpersonally, it is considered a dyadic characteristic, not an individual feature. In fact, a young child's attachments may be different with different caregivers. Infants often develop attachments to more than one caregiver, and develop a hierarchy of preferred attachment figures. Though not well studied, our experience suggests that one to four attachment figures are typical for young children in the United States.

To summarize, infants develop attachments to caregivers whom they have learned are reliably available for comfort, support, nurturance and protection through a period of significant social interaction. Attachment patterns can be organized into one of four attachment classifications (secure, insecure–avoidant, insecure–resistant, and disorganized) that represent the balance of

the child's exploratory, sociable, wariness, and attachment systems. A healthy attachment relationship allows a child to develop an adaptive way to understand the relationship between the world, the self, and others.

ATTACHMENT IN PRESCHOOLERS

A child's expectations regarding the availability and responsiveness of attachment figures are mostly settled by the preschool years. Children at this age have established strategies for managing feelings, such as anger, fear, and the desire for closeness or comfort. These strategies are based on an internal working model of how emotional regulation of the self is best achieved through interaction with the caregiver. Healthy relationships at this age include aspects of warmth, empathy, nurturance, trust, and security. The attachment system continues to play an important role in protecting children from danger, as children learn the value of vigilance and self-protection.

Preschool children, whose cognitive and linguistic skills are substantially more advanced than those of infants in the first or second year of life, seek opportunities to communicate with their attachment figures regarding their mutual access to one another. Without such communication, even children who expect, based upon past experiences, that their attachment figures will be available, if needed, may feel both anxiety and anger. Preschoolers increasingly organize their interactions with attachment figures on the basis of conversations about separations, reunions, feelings, shared activities, and plans, in addition to already established physical and emotional cues. A child's behavior becomes understood in terms of its function in the context of the dyadic relationship (instead of understanding behavior as it directly relates to the attachment pattern). A child's strategy for interacting with a caregiver becomes the defining feature of attachment.

ATTACHMENT DISORDERS IN FORMAL NOSOLOGIES

Disorders of attachment are distinct from the attachment classifications described earlier. They are derived from clinical research with children who have experienced serious deprivation rather than the developmental research that led to attachment classifications.

Descriptive studies of institutionalized children in the mid-20th century defined the phenotypes of contemporary attachment disorders (Goldfarb, 1945; Levy, 1947; Spitz, 1945; Provence & Lipton, 1962; Tizard & Rees, 1975). Studies documenting aberrant social behavior in young, maltreated children also informed evolving criteria (Gaensbauer & Sands, 1979; Gaensbauer & Harmon, 1982; George & Main, 1979).

The first appearance of RAD in diagnostic nosologies was in DSM-III (American Psychiatric Association, 1980). This early version of the disorder

included growth failure and lack of social responsivity as central features. The diagnosis had to have its onset by 8 months of age, which is the age at which preferred attachment is usually just beginning to be evident. Gross neglect of the infant's physical and emotional needs had to be evident. Behaviors indicative of RAD included poor tone, weak cry, excessive sleep, lack of interest in the environment, and weak rooting and grasping when feeding. This appeared to confound RAD with what was called "nonorganic failure to thrive." Although severe neglect may lead to growth failure and disorders of attachment, there is no evidence of a direct link between attachment and failure to thrive; that is, most children with growth failure do not have RAD, and most children with attachment disorders are not failing to thrive. For children who have both conditions, both diagnoses should be made.

In DSM-III-R (American Psychiatric Association, 1987), criteria for attachment disorders were substantially revised. The link between failure to thrive and RAD was dropped, and the age of onset was changed to the first 5 years of life. Two subtypes of the disorder, an emotionally withdrawn/inhibited subtype and an indiscriminately social/disinhibited subtype, were introduced for the first time. In addition, pathogenic care was added as a required etiology.

These changes persisted in DSM-IV (American Psychiatric Association, 1994) and were maintained in other nosologies of early childhood disorders: the Research Diagnostic Criteria—Preschool Age (AACAP Task Force on Research Diagnostic Criteria: Infancy and Preschool, 2003) and in DC:0–3R (Zero to Three, 2005). In contrast, the 10th edition of the *International Classification of Diseases* (ICD-10; World Health Organization, 1992) defined RAD (analogous to the emotionally withdrawn/inhibited subtype in DSM-IV) and disinhibited attachment disorder (analogous to the indiscriminately social/disinhibited subtype in DSM-IV).

Curiously, all of these definitions and their revisions were made in the absence of research designed to validate the criteria. Only in the past two decades has research relevant to the questions of how best to define attachment disorders become available (Zeanah & Gleason, 2015). This research led to the definitions of RAD and DSED in DSM-5, as well as the decision to separate one disorder with two subtypes into two distinct disorders.

REACTIVE ATTACHMENT DISORDER

RAD is characterized by absent or significantly underdeveloped attachment between a child and *all* potential caregivers due to social neglect and deprivation. Children with RAD are believed to be able to form selective attachments, but they have lacked the opportunity due to insufficient caregiving (e.g., being reared in large, impersonal institutions). These children fail to demonstrate attachment behaviors and may appear emotionally withdrawn or inhibited, fail to seek or respond to comfort when distressed, have reduced social and emotional reciprocity, or have disturbances in emotional regulation.

Attachment behaviors, such as seeking proximity to caregivers for safety, support, or comfort, are diminished or absent, even in times of significant emotional distress. Children with RAD rarely "check back" with adults when put in new situations and may not explore their environment. These children display limited positive affect and often appear unresponsive. When approached by possible caregivers, children can appear highly ambivalent about the interaction and resist comforting. Emotional regulation (which develops from interactions with an attachment figure) is impaired, and children may display fear, sadness, or irritability that is not readily explained (American Psychiatric Association, 2013). Many children with RAD display "stereotypies," a movement disorder that develops in association with restricted sensory environments (Bos, Zeanah, Smyke, Fox, & Nelson, 2010).

RAD can only be diagnosed in children exposed to seriously adverse, emotionally neglectful caregiving environments. The disorder has been described both in institutionalized children (Tizard & Rees, 1975; Zeanah, Smyke, Koga, & Carlson, 2005) and in neglected children (Boris et al., 2004; Zeanah et al., 2004). To be diagnosed, children must be at a developmental age at which selective attachments can be formed, meaning a cognitive age of 7–9 months.

DISINHIBITED SOCIAL ENGAGEMENT DISORDER

Like RAD, DSED requires a history of a seriously adverse caregiving environment. DSED has been observed in institutionalized children (Zeanah, Smyke, & Dumitrescu, 2002), children adopted out of institutions (O'Connor & Rutter, 2000), and maltreated children placed in foster care (Zeanah et al., 2004). Despite being exposed to similar environments, children with DSED have very different symptoms than children with RAD.

The defining feature of DSED is socially disinhibited or overly familiar behavior with unfamiliar adults. Children with DSED may approach unfamiliar adults without wariness, appear overly intrusive, violate expected social and physical boundaries, or wander away from caregivers without checking back. Starting around ages 7–9 months, most children maintain proximity to caregivers in new environments and warm slowly to new adults. In contrast, children with DSED immediately approach and engage strangers. These children may have bright affect or appear "more social"; however, the degree of "friendliness" they display is inconsistent with social norms and is often described as uncomfortable or intrusive (Zeanah & Gleason, 2015). Children with DSED may greet an unfamiliar adult with a hug or immediately sit on his or her lap. Initiating physical contact with strangers is rare in children without a history of neglect, and its presence can help to differentiate DSED from age-appropriate exploratory behavior (Lawler, Hostinar, Shanna, & Gunnar, 2014).

Caregivers sometimes express concern that their child with DSED might wander off or leave with a stranger. This appears to be a valid concern: In

a controlled, observational procedure, Gleason, Fox, Drury, Smyke, Egger, et al. (2014) found that 4½-year-old children with a history of institutional rearing were significantly more willing to leave their homes with an unknown adult than were family-reared children.

CLINICAL–DEVELOPMENTAL DIVERGENCE: RAD, DSED, AND CLASSIFICATIONS OF ATTACHMENT

What distinguishes disorders of attachment from classifications of attachment? "Disorders of attachment" (RAD and DSED) are clinical conditions that describe profound disturbances in the child's behavior, both with familiar caregivers and with unfamiliar adults (O'Connor & Zeanah, 2003; Zeanah et al., 2011). Although signs of RAD and DSED may vary in intensity, they are present across all interactions, with different individuals and in different situations. Disorders of attachment are diagnosed by obtaining a history of the child's experiences and behaviors and by clinical assessment of aberrant behaviors that exist within the child and are expressed cross-contextually. These disorders require treatment. Classifications of attachment (secure, avoidant, resistant/dependent, disorganized/controlling, and insecure other), by contrast, are derived from the child's behavior in a laboratory procedure (the SSP) and may be relationship-specific (different with different caregivers). They may or may not suggest a need for preventive interventions (not treatment).

Still, there may be some similarities in the behavior of children with a clinical disorder of attachment and with one or another classification of attachment. For example, similar to RAD, children with avoidant attachments may seem to lack comfort-seeking behaviors, and children with resistant attachments may seem to display emotion regulation problems; however, neither classification of attachment shows the pervasive lack of preference, affective disturbance, and lack of responsiveness that is seen in RAD. Additionally, attachment patterns observed in laboratory paradigms, such as the Strange Situation, should not be used solely to make broad clinical diagnoses (e.g., RAD and DSED).

Children with signs of DSED may or may not have preferred attachments to anyone. In fact, children with DSED may have no attachments, disorganized attachments, insecure attachments, or even secure attachments (Bakermans-Kranenberg, Dobrova-Krol, & van IJzendoorn, 2011; Bakermans-Kranenburg, Steele, et al., 2011; Zeanah & Gleason, 2015). Gleason, Fox, et al. (2011) reported that approximately half of children with indiscriminate behavior following severe deprivation demonstrated organized attachment patterns. Other studies have shown that indiscriminate behavior persists after children develop organized attachments with adoptive parents (O'Connor, Marvin, Rutter, Olrick, & Brittner, 2003) and in children in foster care (Boris et al., 2004). Therefore, some have suggested that DSED may be better conceptualized as a disorder of social engagement than as an attachment disorder

(see Zeanah & Gleason, 2015), though others have argued that the presence of indiscriminate behavior in securely attached children may indicate a lack of true security (see Lyons-Ruth, 2015).

RISK FACTORS FOR RAD AND DSED

Although to develop RAD or DSED children must experience serious neglect or maltreatment in early childhood, most children in these environments do not develop either disorder (Gleason, Fox, et al., 2011). It is not clear what risk factors increase the probability of developing RAD or DSED, although this is currently being explored. The length, severity, and timing of neglect appears to play a role. O'Conner and Rutter (2000) found that children with indiscriminate behavior at age 6 had been institutionalized nearly twice as long as children without indiscriminate behavior at that age, suggesting that longer periods of time in a neglectful environment increase risk. The severity of social neglect also confers risk, perhaps by limiting opportunities to develop attachment to a specific caregiver. This has been demonstrated in institutionalized children who are exposed to more caregivers (allowing less time for a child to bond with a specific person) and in children with more frequent placement disruptions in foster care (Smyke, Dumitrescu, & Zeanah, 2002; Pears, Bruce, Fisher, & Kim, 2010). There are mixed results as to whether subsequent placement of a child with DSED into a high-quality caregiving environment may diminish established symptoms (Lyons-Ruth et al., 2009; Smyke et al., 2012; Van Den Dries et al., 2012).

The timing of neglect is also likely to be important. Children adopted before age 6 months or after 24 months are far less likely to develop indiscriminate behavior (Rutter et al., 2010), although more data are needed to determine whether there is a "sensitive period" during which children are especially vulnerable to neglect (Zeanah & Gleason, 2015).

Studies that examine at prenatal and genetic factors are relatively new. Preliminary genetic studies have shown changes in the serotonin transporter gene (*5-HTT*) and in brain-derived neurotropic factor (BDNF) may impact a child's susceptibility to developing an attachment disorder (Drury, Gleason, et al., 2012). In another study, Drury, Theall, et al. (2012) noted that children who had spent time in an institution had shorter average telomere length than children who had not. The stress of institutional rearing may result in epigenetic changes that impact future health, regardless of whether a child develops an attachment disorder.

NEUROBIOLOGY

An increasing number of researchers have examined changes in brain structure and function in children with a history of severe deprivation (see Nelson, Bos,

Gunnar, & Sonuga-Barke, 2011; Nelson, Fox, & Zeanah, 2014). Although these studies do not focus exclusively on children with attachment disorders, examination of this broader group of children has been helpful in identifying some of the biological consequences of early, severe neglect.

Brain structure and functioning appear to be altered by early experiences of deprivation, at least for those exposed for significant periods of time, and especially after 6 months of age. Consistent findings from children raised in institutions, for example, are reductions in both gray- and white-matter volumes (Eluvathingal et al., 2006; Mehta et al., 2009; Sheridan, Fox, Zeanah, McLaughlin, & Nelson, 2012). These reductions are accompanied by reduced electrical activity in higher frequencies and increased electrical activities in lower frequencies (Marshall, Fox, & the BEIP Core Group, 2004; Marshall, Reeb, Fox, Nelson, & Zeanah, 2008; Tarullo, Garvin, & Gunnar, 2011; Vanderwert, Marshall, Nelson, Zeanah, & Fox, 2010). Less clear is how lasting these changes may be, but for children removed from deprived institutional settings and placed in foster care before 24 months, Vanderwert et al. (2010) demonstrated normalization of brain functioning by age 8 years.

Preliminary researchers looking for specific anatomical changes have reported decreased amygdala volume and disruptions of the connectivity between the amygdala and the prefrontal cortex (Mehta et al., 2009; Sheridan et al., 2012; Olsavsky et al. 2013). This may have important implications for emotion regulation and executive functions, as do memory, attention, and planning. Neuropsychological testing of institutionalized children has shown some correlation to anatomic findings, reporting lower IQ scores and deficits in memory, attention, inhibitory control, and executive function (Nelson et al., 2011). Electroencephalographic studies show alteration in the power of high and low frequencies that may reflect delayed brain maturation (Nelson et al., 2011).

Some of these findings appear to be dependent on the length of exposure to deprived environments. In the English and Romanian Adoptees Study, many children's head circumferences normalized by adolescence after placement in foster care, but children with longer histories of institutionalization often remained significantly below the norm (Sonuga-Barke et al., 2008). These findings are exciting and may offer a better understanding of the effects of neglect; however, they are relatively new and should be considered preliminary until the studies can be replicated. Additional work also is needed to determine the specific circuitry affected in association with the phenotypic pictures of RAD and DSED.

PREVALENCE OF RAD AND DSED

The prevalence of RAD and DSED are unknown, but both disorders appear to be rare. The limited data that are available have focused on children raised

in high-risk settings, such as institutional care and subsequent foster care. In a longitudinal study examining children with a history of severe neglect in Romanian institutions, the incidence of RAD was less than 5%, and the incidence of DSED was less than 20% (Gleason, Fox, et al., 2011). Still, the number of children who are at risk for these disorders due to inadequate caregiving is alarmingly high. In the United States, 1.5 million children experience homelessness in a year (Bassuk, 2009). There are approximately 700,000 unique cases of child abuse and neglect confirmed by Child Protective Services annually, and the actual number of victims is likely much higher (U.S. Department of Health and Human Services, Administration for Children and Families, Children's Bureau, 2013). Controversies regarding the definition of each disorder at different developmental stages and other measurement challenges remain obstacles to assessing prevalence accurately.

COURSES OF RAD AND DSED

RAD and DSED appear to have different courses. Most of the data on the course of RAD comes from one study, the Bucharest Early Intervention Project (BEIP). In that study, RAD was readily identifiable in infants and preschool-age children living in Romanian institutions (Zeanah et al., 2005). Without intervention, children in this study continued to show symptoms of RAD a few years later, at ages 4–5 years (Gleason, Fox, et al., 2011). Symptoms rapidly dissipate when children are removed from an institution and placed in a supportive environment (Smyke et al., 2012). According to one descriptive study, children may begin to organize attachments to new caregivers within days of placement in a new setting (Stovall & Dozier, 2000). RAD has not been identified in children recently adopted out of institutions in two longitudinal studies of formerly institutionalized children (O'Connor & Rutter, 2000; Chisholm, 1998), probably because the follow-ups were months after adoption, when symptoms had diminished.

DSED has a variable course but can be persistent. Many children in the BEIP continued to have symptoms regardless of whether they remained in an institution or were placed into foster care (Gleason, Fox, et al., 2011). Children with DSED may continue to demonstrate indiscriminate behavior even after developing a selective attachment to their adoptive parent (Chisholm, 1998; O'Connor et al., 2003). In one of the first studies on this subject, Tizard and Rees (1975) described overly friendly and attention-seeking behavior in 4-year-old children with a history of institutionalization. They found that these same children had persistent symptoms of indiscriminate behavior at 8 years old (Tizard & Hodges, 1978). At 16 years old, these children, although no longer indiscriminate, were found to be superficial with peers and to report more peer conflicts than children who did not display indiscriminate behavior (Hodges & Tizard, 1989). This may reflect a different behavioral expression of the same disorder over time.

In both DSED and RAD, some symptoms may resolve, but it is not clear whether affected children will continue to have long-term problems with social skills, emotional regulation, or other sequelae into adulthood. Studies of children adopted out of institutions reveal that more than 40% of children exhibit insecure attachment patterns several years after adoption (Chisholm, 1998; Marcovitch, Goldberg, Gold, Washington, Wasson, et al., 1997; O'Connor et al., 2003). The consequence of this finding is unknown. Preliminary studies have shown children with RAD and DSED have functional impairment, social impairment, and increased use of health and special education resources in early childhood (Chisholm, Carter, Ames, & Morison, 1995; Rutter et al., 2010; Gleason, Fox, et al., 2011), but long-term follow-up is needed.

Without prospective studies beginning in early childhood, it is difficult to examine RAD and DSED in older children. The criteria used to define and study both RAD and DSED are almost exclusively based on data from children younger than 6 years old. Some researchers looking at RAD and DSED in late childhood and adolescence define the disorders more broadly. It is important to note that there is controversy as to whether these definitions accurately reflect the same disorders that have been studied in younger children.

ASSESSMENT OF RAD AND DSED

No established protocol exists for diagnosing RAD or DSED. There is, however, promising support for the utility of structured observations and interviews (Zeanah et al., 2011; Zeanah, Chesher, & Boris, in press). Structured episodes that activate the attachment system, such as Strange Situation separations, allow clinicians to observe attachment behaviors and to contrast behavior toward an attachment figure and a stranger. Observation of the infant's responses toward caregivers and toward strangers throughout all other parts of the assessment is also essential. However, as outlined earlier, deriving an attachment classification from the Strange Situation alone does not allow diagnosis of an attachment disorder. The SSP is neither necessary nor sufficient for diagnosing attachment disorders, but it may be a useful procedure in some settings. Unfortunately, at this point, there is no "gold standard" procedure beyond expert clinical assessment to diagnose or classify either RAD or DSED definitively.

Lack of attachment behaviors in the Strange Situation have been associated with RAD in institutionalized infants (Smyke et al., 2002; Zeanah et al., 2005), although, in a clinical context, all putative attachment figures would need to be assessed, since absence of attachment behaviors directed toward one caregiver cannot preclude presence of attachment behaviors with another caregiver. Although some observational research paradigms show promise (Boris et al., 2004), the current standard for clinical assessment includes observation of free play with caregivers and arousal of the attachment system by separations and reunions with caregivers and strangers to determine

whether the child (1) becomes distressed, (2) uses the caregiver or others for comfort, and/or (3) has a clear preference for the caregiver.

A number of observational paradigms have been used to identify signs of DSED. These have ranged from coding behavior toward the stranger in the SSP (Lyons-Ruth, Bureau, Riley, & Atlas-Corbett, 2009; O'Connor et al., 2003) to other laboratory paradigms (Lawler et al., 2014) to observations of behavior with strangers in the home (Gleason et al., 2014). The substantial convergence between observational paradigms and caregiver interviews increases confidence that the same construct is being assessed (Zeanah & Gleason, 2015).

Likewise, although there is no "gold standard" interview, the Disturbances of Attachment Interview (Smyke et al., 2002) has demonstrated the usefulness of semistructured clinical interviews in the identification of disordered attachment and indiscriminate social behaviors (Smyke et al., 2002; Smyke et al., 2012; Gleason, Zamfirescu, et al., 2011; Zeanah et al., 2005). Whatever interviews are used should cover all of the possible symptoms associated with all descriptions of RAD and DSED, and explore both the contextual determinants and the course of these behaviors.

At present, we recommend detailed observations in naturalistic and clinical settings, as well as obtaining multiple focused reports from caregivers. This approach must suffice until further empirical clarifications of the diagnostic features are available. At this point, it is most important to observe general social relatedness, as well as specific attachment behaviors between the preschooler and the primary caregivers.

COMORBIDITY/DIFFERENTIAL DIAGNOSIS

Developmental Delays

Children must experience significant neglect or maltreatment to be diagnosed with RAD or DSED. This same type of neglect also puts children at risk for developmental delays, and because of this shared etiological factor, comorbidity is common. It is therefore critical to test a child's development, including language evaluation, as a routine part of the assessment.

Attachment disorders, especially RAD, can occasionally be confused with developmental delay. In order to diagnose RAD or DSED, a child must be at a *developmental age* at which attachments can be formed. Children with developmental delays (who do *not* have RAD or DSED) should exhibit social and emotional skills appropriate for their cognitive age. They will also form selective attachments when they reach a developmental age of 7–9 months.

Autism Spectrum Disorders

Distinguishing between RAD and autism spectrum disorders (ASD) can be a diagnostic challenge. Preschoolers with either ASD or RAD may demonstrate

limited social reciprocity, limited positive affect, and poor emotional regulation. Both groups of children may also have cognitive delays and stereotypies. According to DSM-5, ASD and RAD cannot be comorbid, though this requirement has been criticized (Zeanah, 1996).

RAD and ASD can be differentiated by history and clinical symptoms, and by observing the response to intervention. Children with RAD typically have significant improvement in symptoms with placement in a secure environment, while those with symptoms of ASD will remain unchanged. In addition, most children with ASD will *not* have a history of social deprivation. Children with ASD also have behaviors that are not typical of RAD, including repetitive behavior, restricted interests, deficits in joint attention, selective language abnormalities, and selective impairment in symbolic play. Children with ASD should have a selective attachment to their caregiver.

Posttraumatic Stress Disorder

Children diagnosed with RAD or DSED may have experienced significant maltreatment, including witnessing or being the victim of frightening or abusive experiences. It is important to differentiate symptoms of hyperarousal, avoidance, and changes in affect related to posttraumatic stress disorder (PTSD) from the emotional blunting and dysregulation of RAD. The natural course of each disorder may be helpful in differentiating the two. RAD typically improves rapidly in a supportive environment, while PTSD often does not remit without treatment. The disorders may be comorbid, and careful consideration of both disorders is warranted in children who are victims of neglect or abuse.

Conduct Disorder

Historically, some adolescents with violent or callous behavior have been diagnosed with RAD. There is, however, no clear relationship between psychopathy and RAD, although data are less clear about DSED. The ICD-10 (World Health Organization, 1992) includes the term "affectionless psychopathy" as one manifestation of disinhibited attachment disorder (similar to DSED). This inclusion in ICD-10, but not DSM-5, highlights the debate over heterotypic continuity and how DSED is defined in older children.

Attention-Deficit/Hyperactivity Disorder

Children with DSED may wander off, appear talkative with strangers, or violate conventional physical boundaries; children with attention-deficit/hyperactivity disorder (ADHD) may demonstrate similar behaviors due to impulsivity. Differentiating between the two disorders may be difficult in certain cases. Studies have shown that symptoms of DSED may be associated with symptoms of ADHD (Gleason, Zamfirescu, et al., 2011), but they remain distinct clinical

entities. Typically, children with DSED should not demonstrate the inattention or hyperactivity characteristic of ADHD. Nevertheless, ADHD is relatively common, and some children may meet criteria for both disorders.

INTERVENTIONS FOR RAD AND DSED

There are limited data on the treatment of RAD and DSED. Most studies to date have been retrospective or naturalistic, with the exception of one randomized controlled trial (BEIP). The available data support early intervention that addresses the history of neglect. The most important step is to provide a child with the opportunity to bond with an emotionally available attachment figure.

First, a provider must always assess the safety of the child's current environment. Children with RAD and DSED have universally been exposed to neglect in early childhood and may have ongoing and exposure to abuse, neglect, or maltreatment. If the child's safety cannot be ensured, removal of the child from the home is mandated by law in all 50 states. Although placement in foster care disrupts the child's relationship with the primary caregiver, safety must be established as the first priority.

The next step is to provide the child with the opportunity to bond with an emotionally available attachment figure. If the child needs to be moved to foster care, this should be done as quickly as possible, because the younger the age of placement, the less likely a child is to develop a disturbed attachment. The role of the provider is to work with the caregiver and help him or her foster an attachment with the child. Zeanah (Smyke, Wajda-Johnston, & Zeanah, 2004; Zeanah & Smyke, 2005) and others (Dozier, Lindhiem, & Ackerman, 2005) have outlined approaches designed to facilitate this attachment. These approaches emphasize working with the child and caregiver together and, if necessary, helping the child gradually transition to a new caregiving environment. The clinician can provide psychoeducation about symptoms, teach about sensitive caregiving, and facilitate positive interactions with a sometimes-difficult child. The most important components to developing a healthy attachment are sensitive caregiving and a caregiver's psychological investment in the child (Smyke et al., 2012).

Some important barriers to treatment include caregiver depression, substance abuse, unresolved trauma/loss, and domestic violence. Immediate referral to address these concerns is warranted. Treatment of comorbid behavioral problems in the child is also important. Caregivers frequently highlight disordered sleep and feeding behaviors, tantrums, and aggression as barriers to mutually rewarding relationships.

Several psychotherapeutic approaches have been used to help caregivers and children develop healthier attachments, and three attachment-based interventions are discussed below, including child–parent psychotherapy, interaction guidance, and the Circle of Security. Although no studies to date

have evaluated specific psychotherapeutic approaches for young children with RAD or DSED, therapies that focus on the caregiver–child relationship have been effective in treating children with insecure or disorganized attachment relationships (see Zeanah, Berlin, & Boris, 2011, for review).

Child–parent psychotherapy (CPP) is a type of parent–child relational therapy that combines insight-oriented psychotherapy, emotional support, and direct guidance to caregivers and their toddlers. The therapy focuses on how the caregiver and child experience one another and their patterns of communication. The therapist provides corrective reinterpretation of the parent and child's signaling to one another, and the members of the dyad learn to interpret each other differently. The goal is to improve the caregiver–toddler relationship and the child's social and emotional functioning. Children and parents also learn developmentally appropriate interactions and affect regulation.

Interaction guidance (McDonough, 2004) is a dyadic therapy designed to meet the needs of families that previously have not been successfully engaged in treatment and may be overburdened by poverty, lack of education, large family size, substance abuse, inadequate housing, and lack of social support. The interaction guidance approach assists family members in gaining enjoyment from their relationships with their children and in developing an understanding of their children's behavior through an experience of interactive play. Via immediate and reflective viewing of videotaped play interactions, the caregivers are praised for their appropriate interactive strengths. Parent-initiated discussions of more troublesome interactions may also become a focus of treatment.

The Circle of Security is an eight-session therapy designed to teach parents in high-risk dyads the basics of attachment patterns to facilitate a change in attachment behaviors (Powell, Cooper, Hoffman, & Marvin, 2013). Caregivers watch edited videotapes of their interactions with their children and learn to increase their sensitivity and responsiveness to their children's signals. The treatment focuses on increasing caregivers' ability to reflect on their own behavior, thoughts, and feelings when they are interacting with their children. Caregivers learn to interpret how their own life experiences can affect their attachment relationship with their children.

In some cases, the same caregiver who exposed the child to neglect may be involved in the treatment, either as the current caregiver or with a plan for reunification after a temporary placement in foster care. This is a common scenario in children referred to care by Child Protective Services or court order. These types of cases require evaluation of the original caregiver and the foster parent to determine the appropriateness of the current placement. Important factors to take into account when considering the fit of a caregiver include his or her interest in the child, sensitivity to the child's needs, motivation to care for the child, as well as the family support, stability, and means to care for child. If the caregiver responsible for the original neglect or abuse remains involved, it is also important to consider the caregiver's willingness to

take responsibility for his or her impact on the child, response to any previous interventions, and the type, severity, and pattern of past abuse. See Martinez-Tortega, Rosenblum, and Marcus (Chapter 13, this volume) for a detailed overview of attachment-based therapies.

When attempting to determine whether a caregiver is a good fit for a child, structured interviews can be helpful. Certain caregiver responses to two structured interviews—the Adult Attachment Interview (AAI) and the Working Model of the Child Interview (WMCI)—are predictive of a parent developing a secure attachment with a child. The AAI asks 20 questions about an adult's attachment to his or her family of origin. Foster parents who have autonomous narratives are more likely to develop secure attachments with their foster children (Dozier, Stovall, Albus, & Bates, 2001). The WMCI (Zeanah & Benoit, 1995) assesses a caregiver's representation of the child and his or her relationship with that child. Balanced narratives from this measure are similarly associated with secure attachment. These interviews assess the caregiver's ability to discuss and reflect upon caregiving experiences (AAI) and his or her ability to take an emotional perspective on the child's experiences, circumstances, personality, and his or her own relationship with that child (WMCI). Insight into the caregiver's attachment style can provide a therapeutic platform for a clinician to work with the parent.

The child's best interest should remain the primary focus throughout the evaluation. If a child is placed in foster care and reunification is not possible, the child should be freed for adoption immediately in the hope of expediting permanent placement. Disruptions in placement can be very disturbing to young children and should be kept to a minimum. Treatment should also consider the child's social circumstances. Children with RAD and DSED typically come from impoverished settings and may require multiple social agencies to address their needs. This may be approached through an organized community system of care (Marx, Benoit, & Kamradt, 2003; Klaehn & Martner, 2003), including case management, social services, and agencies that work with children at risk for developmental delays.

TREATMENTS TO BE AVOIDED

Although the empirical evidence base for treatment of RAD and DSED remains small, there is a group of treatments that should be avoided, including "attachment therapy," "holding therapy," "rage reduction therapy," "rebirthing therapy," and similar treatments. These therapies are usually based around coercion and physical restraint, reworking of "forgotten" early childhood trauma, and developing "reattachment." These types of therapy are not evidence-based; they are outside the scope of typical practice, are unlikely to be helpful, and may be physically or psychologically harmful. They are also not consistent with attachment theory or our current understanding of RAD and DSED.

It is also important to note that there is no evidence that any medication can treat the core features of RAD or DSED, though some children may have comorbidities that warrant pharmacological treatment.

CONCLUSIONS

The attachment system motivates young children to seek comfort, support, nurturance, and protection. In the preschool years, it forms the foundation of relationships and affects how children view themselves, others, and the world. Children exposed to severe neglect or maltreatment in early childhood have limited opportunity to form attachments.

RAD and DSED are distinct disorders that arise from significant neglect. It is not clear why similar circumstances lead to two disorders that have different clinical pictures, courses, responses to intervention, and sequelae. Future research may help to clarify the etiology of these disorders, their longitudinal course, and more effective ways to treat them. Currently, children with either disorder are best served by placement in a secure environment where they may have the opportunity to develop a secure attachment to a caregiver.

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10

Sleep Disorders

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> It is 2:00 A.M. and the family is exhausted. Two-year-old James is still screaming. He cannot settle to sleep. His parents, sleep-deprived themselves, are at their wits' end. They have not had a good night's sleep since his birth. They argue about what to do, especially since all of the advice they have received from popular books, parents, friends, and even their physician has been contradictory and to no avail. What to do? Let him scream? Take him into their bed to comfort him? What else?

In this chapter we review empirical data and clinical experience about young children's sleep problems to better inform clinicians who treat infants through preschool-age children and their families. We first review normal development of sleep–wake patterns, with a focus on the interactions of biological and maturational factors with psychosocial and environmental factors. Next, we review the types of sleep problems in this age group and review some of the suspected daytime behavioral concomitants of nighttime sleep disruption and other sleep disturbances. We discuss some of the issues related to classification of sleep disorders at these ages and present our own classification scheme as a potential nosology deserving further research. Finally, we briefly discuss and conclude with some suggestions for best practices regarding both prevention and treatment of sleep problems in this age group.

NORMAL DEVELOPMENT OF SLEEP–WAKE PATTERNS FROM BIRTH THROUGH THE PRESCHOOL YEARS

The relatively short period between birth and the preschool years involves considerable changes in the patterns and structure of sleep and wakefulness. Not only does diurnal rhythmicity emerge, but changes occur also in the proportions of time young children spend in each sleep state, in the amount of time they spend asleep, and in the distribution of that sleep across the 24-hour day. Although many of these changes are maturational, the environmental context to which young children are exposed has been shown to impact the development of sleep and waking patterns. For instance, maternal well-being, parental ideology, and cultural beliefs impact the sleep setting, as well as the quality and development of typical sleep–wake patterns. Therefore, a large degree of individual variability marks the development of sleep, complicating the attempt to describe what is "normal." Each of these developmental and environmental factors is discussed briefly in an effort to describe the range of normal development in sleep over the course of the first 5 years of life.

Changes in Sleep Patterns and Sleep Structure

Research over the past 60 years has shown that the characteristics of sleep change with development. These changes occur in not only in the amount of sleep but also sleep structure. Detailed study of infant sleep in the 1950s served to supplant several myths that prevailed in the early part of the century. For example, it was discovered that during the newborn period, infants sleep approximately 16–17 hours per day, in sharp contrast to the estimated 20–22 hours that had been reported in pediatric textbooks prior to the 1950s (Kleitman & Engelmann, 1953; Parmelee, Schulz, & Disbrow, 1961). It also had been generally accepted that the total amount of sleep declines early in infancy. Kleitman and Engelmann's (1953) seminal longitudinal work, however, showed that the total duration of sleep did not differ over the first 3–6 months of life; rather, the distribution of sleep over the 24-hour day changed. This finding was substantiated in subsequent investigations (Anders & Keener, 1985; Parmelee, 1961; Parmelee, Wenner, & Schulz, 1964). While the total amount of 24-hour sleep has been found to remain quite stable, the longest continuous sleep period has been found to increase during this time period, from 3–4 hours at birth to 6 hours on average by 6 months (Anders & Keener, 1985; Burnham, Goodlin-Jones, Gaylor, & Anders, 2002; Campbell, 1986; Coons & Guilleminault, 1984; Parmelee, Wenner, & Schultz, 1964). Beyond the first 3–6 months, total sleep time decreases to 14–15 hours in 24 hours by the age of 1 year. In contrast, the longest continuous sleep period remains constant at 6–7 hours for the remainder of the first year (Anders & Keener, 1985; de Roquefeuil, Djakovic, & Montagner, 1993; Jacklin, Snow, Gahart, & Maccoby, 1980; Parmelee, 1961). This general pattern of change in amount and consolidation of sleep has held across a number of studies using different

methodologies (e.g., Iglowstein, Jenni, Molinari, & Largo, 2003). During the toddler and preschool period, as naps are given up, total 24-hour sleep time is reduced even more. However, the amount of nighttime sleep remains constant or increases slightly.

Developmental research has revealed not only these changes in sleep amounts during infancy but also changes in sleep structure. Interestingly, the oscillations between active and quiet sleep were first observed in infants as early as 1924 by Denisova and Figurin (Anders, 1975). Their publication in an obscure European journal, however, precluded these findings' wide disseminated. In the 1960s, polysomnographic equipment and sleep scoring procedures were adapted for use with infants and confirmed the findings derived from behavioral observations indicating developmental patterns in the amount and distribution of active and quiet sleep periods (e.g., Roffwarg, Dement, & Fisher, 1964; Roffwarg, Muzio, & Dement, 1966). (In the young infant, active sleep is the precursor of rapid eye movement [REM] sleep and quiet sleep is the precursor of non-REM [NREM] sleep seen in the older child and adult.) These early studies revealed the unanticipated finding that newborns spent a much larger proportion of time in active sleep compared to adults (Roffwarg et al., 1966). Both behavioral and physiological measures of infant sleep have revealed that the percentage of time spent in active sleep decreases over the first year of life, while there is a concomitant increase in quiet sleep (Anders & Keener, 1985; Burnham et al., 2002; Dittrichová, 1966; Emde & Walker, 1976; Fagioli & Salzarulo, 1982; Harper et al., 1981; Louis, Cannard, Bastuji, & Challamel, 1997; Navelet, Benoit, & Bouard, 1982; Thoman & Whitney, 1989). Furthermore, the cycle length between active and quiet sleep is shorter than the 90-minute cycle that is characteristic of adult sleep. Cycling between active and quiet sleep occurs approximately every 50–60 minutes in infancy (Aserinsky & Kleitman, 1955; Dittrichová, 1966; Harper et al., 1981). The 90-minute pattern is not evident even by 2 years of age (Louis et al., 1997). Roffwarg and colleagues (1964) reported that the adult cycle length begins to appear in middle childhood, indicating a prolonged period of maturation.

Sleep Consolidation

Perhaps the most explicit change occurring in infant sleep is the increased consolidation of sleep to the nighttime period, which occurs in the first few months of life. A good literature base has examined the development of the sleep–wake rhythm during early infancy. The bulk of these studies suggest that diurnal variation between sleep and waking, with most sleep becoming consolidated to the nighttime hours, is well established by the age of 3 months (Bamford et al., 1990; Burnham, 2007; Coons & Guilleminault, 1984; Hellbrügge, Lange, Rutenfranz, & Stehr, 1964; Kleitman & Engelmann, 1953; McGraw, Hoffmann, Harker, & Herman, 1999; McMillen, Kok, Adamson, Deayton, & Nowak, 1991; Meier-Koll, Hall, Hellwig, Kott, & Meier-Koll,

1978; Parmelee et al., 1964; Shimada et al., 1999; Sostek, Anders, & Sostek, 1976; Spangler, 1991; Yokochi, Shiroiwa, Inukai, Kito, & Ogawa, 1989), if not earlier (Freudigman & Thoman, 1994; Sadeh, Dark, & Vohr, 1996). Thus, after a period of maturation during the first weeks of life, on average, sleep becomes consolidated to the nighttime hours by the age of 3 months. It is likely that there are individual differences in the development of sleep–wake rhythmicity, as well as sleep times, which may be either endogenous or environmentally induced (e.g., Parmelee et al., 1961; Menna-Barreto, Isola, Louzada, Benedito-Silva, & Mello, 1996; Sander, Julia, Stechler, & Burns, 1972). Although infants do shift their sleep to the nighttime, and they do begin to sleep for longer stretches of time, it is inaccurate to conclude that they "sleep through the night." Indeed, the vast majority of infants continue to awaken during the night, even at 12 months of age (Burnham et al., 2002; Goodlin-Jones, Burnham, Gaylor, & Anders, 2001). What appears to develop over time is infants' ability to "self-soothe/quiet," defined as their ability to put themselves back to sleep upon awakening without waking a parent (Burnham et al., 2002).

Although the majority of sleep consolidation occurs relatively early in life, infants and young children continue to nap during the day until about the age of 4 or 5 years (Iglowstein et al., 2003). By about 18 months of age, a single afternoon nap is typical, whereas younger infants often experience several naps throughout the day. As preschool-age children gradually eliminate the daytime nap, their nighttime sleep durations tend to increase (e.g., Mindell, Sadeh, Weigand, How, & Goy, 2010).

A TRANSACTIONAL MODEL OF SLEEP–WAKE REGULATION

Nightly transitions between waking and sleep at bedtime and during the middle of the night offer opportunities for homeostatic regulation (e.g., hunger, temperature) and social regulation (separation, reunion, comfort) (Anders, Goodlin-Jones, & Sadeh, 2000). Early contingent responsiveness during these transitions presumably facilitates the development of self-regulation and very likely contributes to the emergence of a secure attachment relationship (Adams, Stoops, & Skomro, 2014; Ainsworth, Blehar, Waters, & Wall, 1978). Caregivers' failure to respond consistently and predictably to aid the child during these transitions is associated with less optimal regulation (Teti, Kim, Mayer, & Countermine, 2010). Nevertheless, there is a complex interplay among infant sleep regulation, maternal cognitions regarding the infant, and parental personality (Sadeh, Tikotzky, & Scher, 2010; Tikotzky & Sadeh, 2009). An assessment of sleep in the infant, toddler, and preschool-age child, therefore, necessarily involves assessment of the emerging parent–child relationship and the psychosocial factors that impact that relationship, as depicted in Figure 10.1.

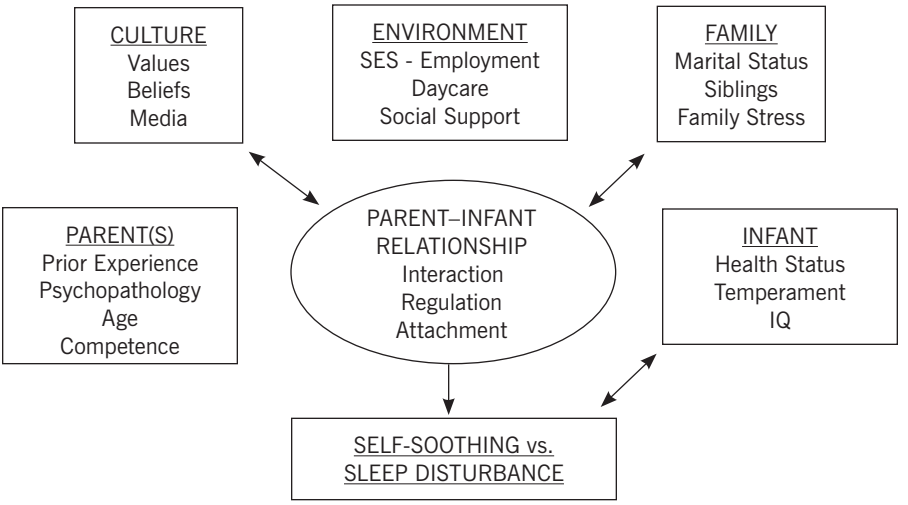

FIGURE 10.1. The transactional model, illustrating the context within which children's sleep develops.

Proximal influences on the relationship include the primary caregiver's current state of physical and psychological well-being; the primary caregiver's own childhood experiences of being parented, including their experiences around sleep; current social support networks; the family's economic and household condition; and the infant's temperament and physical health. More distal factors in the transactional model include the broader cultural context of the family and indirect environmental influences. According to this model, proximal stressors, such as infant physical illness or maternal depression, directly impact parent–child interactions surrounding regulation of sleep and, in turn, these altered interactions affect the family. A more thorough discussion of these influential factors is published elsewhere (Goodlin-Jones, Burnham, & Anders, 2000; Sadeh et al., 2010; Teti et al., 2010).

Thus, although in the past sleep was thought of as a characteristic of the individual, for young children, it is necessary to consider the larger context of their relationships, family, and sleep environments to understand both the development of sleep–wake patterns and the emergence of sleep problems. At this age, a sleep problem often is specific to a particular relationship or setting. A child will nap in the child care setting but not at home (or vice versa), or a child will fall asleep more easily when the babysitter puts him or her to bed than when the parent does (or vice versa). Sometimes, infants and young children respond differently to mothers and fathers.

Conversely, there is the possible impact of childhood sleep problems on maternal mental health, the parent–child relationship, and on the relationship between parents (for an example of families with child with a disability, see

Richdale, Francis, Gavidia-Payne, & Cotton, 2000). For instance, Goldberg and colleagues (2013) found that mothers who reported infant bedtime problems at 6 months reported higher depressive and anxiety symptoms when the infant was 12 months old. However, these authors also found relationships between maternal mental health at infant age 6 months and the degree to which mothers were bothered by bedtime issues when their infants were 12 months old. Given this evidence, the relationship between mental health and sleep problems appears to be complex and transactional in nature. Another example is the possibility that bed sharing that occurs as a reaction to a young child's sleep problems may have a negative impact on family relationships (Ramos, 2003). However, Ball, Hooker, and Kelly (2000) have reported positive effects of bed sharing on paternal nighttime caregiving involvement among a group of parents who did not originally plan to bed-share.

Exacerbating the complexity of the relationships among sleep and other factors is the large degree of individual variability in families' tolerance and definition of "sleep problems" in infancy and early childhood. Those families who define their child's sleep as problematic may be more likely to report family or relationship problems stemming from the sleep problem and are probably most positively affected by interventions designed to alleviate the sleep problem (Eckerberg, 2004).

Some potential contextual influences on the development of sleep–wake patterns include family values and cultural beliefs, parental experience, family stress, maternal well-being, and whether or not mothers choose to breastfeed. A large influence on the development of sleep–wake patterns and rhythmicity is sleep location (Burnham & Gaylor, 2011). Worldwide, the practice of sharing the same bed or room with one's young child is common among parents. Although traditionally thought of as less prevalent in the United States, bed sharing does occur in a significant subgroup of American families (e.g., Hauck, Signore, Fein, & Raju, 2008). One report indicated that 88% of parents of children under the age of 5 admitted to having shared the same bed at some point during the child's life, while a full 46% reported bed sharing for the majority of days during the past month (Weimer et al., 2002). Regardless of whether bed sharing occurs in the United States as a preferred choice of parents or as the reaction to a "problem" with the child's sleep (Ramos, 2003), it is clear that bed sharing is quite prevalent, both during infancy and the preschool years (Jenni, Fuhrer, Iglowstein, Molinari, & Largo, 2005).

There is some evidence that the practice of bed sharing influences the development of sleep. For example, using polysomnography, Mosko, Richard, McKenna, and Drummond (1996) found that infants spent less time in deep sleep (NREM Stage 3–4) and more time in shallower stages of sleep (NREM Stages 1–2) when bed sharing in a laboratory, regardless of the infant's routine sleeping environment. Richard and Mosko (2004) also reported heart rate differences in these infants that were related to the sleep environment, suggesting that sensory differences between the two sleeping environments may account for these distinctions. Both arousability thresholds and heart rates appear to

differ during bed sharing versus solitary sleeping, suggesting that the practice of bed sharing induces a physiologically based response in the infant. Bed sharing also tends to co-occur with the practice of breastfeeding (Ball, 2003; McKenna, Mosko, & Richard, 1997). Breastfeeding has been related to sleep patterns, with infants who are breastfed during the night waking more and requiring more parental interventions upon awakening in the night than those who have been weaned (Burnham et al., 2002).

In addition to differences induced by the sleep context, young children's sleep also may be influenced by family beliefs regarding children's use of sleep aids (objects used for nighttime comfort, e.g., a blanket or pacifier) or when and how to respond to a crying infant. Several studies have shown that young children who use a sleep aid are more likely to soothe themselves to sleep during the night (Anders, Halpern, & Hua, 1992; Goodlin-Jones, Eiben, & Anders, 1997; Keener, Zeanah, & Anders, 1988); and that infants whose parents delay slightly their response to nighttime crying after 3 months of age tend to be self-soothing/quieting infants at 1 year of age (Burnham et al., 2002). With regard to maternal well-being, Seifer, Sameroff, Dickstein, Hayden, and Schiller (1996) reported an association between young children's sleep disruption and maternal mental illness, as well as low levels of family cohesion. Other research has unveiled a relationship between maternal attachment insecurity and sleep problems in toddlers (e.g., Adams et al., 2014).

IDENTIFICATION OF SLEEP DISORDERS IN YOUNG CHILDREN AND EFFECTS ON DAYTIME BEHAVIOR

In general, studies using various criteria to define a sleep problem, either provided by parental report questionnaires or diary methods, demonstrate that approximately 30% of young children have some kind of sleep problem, ranging from mild, time-limited difficulties with bedtimes to chronic, serious sleep disorders, such as obstructive sleep apnea (Archbold, Pituch, Panahi, & Chervin, 2002; Armstrong, Quinn, & Dadds, 1994; Earls, 1980; Jenkins, Bax, & Hart, 1980; Kataria, Swanson, & Trevathan, 1987; Richman, 1981; Ottaviano, Gianotti, Cortesi, Bruni, & Ottaviano, 1996). When parents are asked directly if they think their child has a sleep problem, an epidemiological telephone survey conducted by the National Sleep Foundation (2004) revealed that only 10% of parents report a sleep problem in their preschool-age child. Perhaps this discrepancy represents the individual variation in young children's sleep patterns that in a transactional model interact with parental belief systems about what is "problem" sleep and how to respond to nighttime difficulties. Although difficulties falling asleep at bedtime and frequent and/or prolonged night awakenings are the most common sleep disorders in young children, identification of excessive daytime sleepiness, intransigent behavioral sleep disorders, and more severe, medically based disorders (e.g., obstructive sleep apnea) are extremely important to recognize, because these disorders

can impair physical, cognitive, and psychosocial development. While it is possible that young children with bedtime settling and nighttime awakening problems also experience impaired daytime functioning, research in this area is, unfortunately, lacking.

Types of Sleep Disorders in Childhood

The most recent edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5; American Psychiatric Association, 2013), the *International Classification of Diseases* (ICD, 10th edition; World Health Organization, 1992), and the third edition of the *International Classification of Sleep Disorders* (ICSD-3; American Academy of Sleep Medicine, 2014) do not classify sleep disorders in childhood separately from those in adulthood. This is surprising due to clinical evidence suggesting that differences may exist, and the fact that children often do not meet the adult frequency, duration, and severity thresholds. In this section, we focus on the broad categories and most common sleep disorders seen in the infancy and preschool years. Cortese, Ivanenko, Ramtekkar, and Angriman (2014) have recently completed a thorough review of childhood sleep disorders and their classification.

"Dyssomnia" is a general category of sleep disorder defined by disruptions of sleep. The category includes *intrinsic dyssomnias* (narcolepsy, sleep apnea, and restless leg syndrome) and *extrinsic dyssomnias,* or behavioral sleep disorders (limit-setting sleep disorder and sleep-onset association disorder). Sleep-disordered breathing is considered an *intrinsic dyssomnia* and can, but does not necessarily, include obstructive sleep apnea syndrome (OSAS). Snoring and prolonged mouth breathing during sleep are two cardinal signs that should alert clinicians to this sleep disorder. Obstructed breathing in this age group is most likely due to enlarged tonsils and adenoids, and surgery most often leads to alleviation of the symptoms (Marcus et al., 2013). OSAS peaks between ages 2 and 6 years, when approximately 2–3% of children are diagnosed (Tauman & Gozal, 2011). An even greater percentage (8%) of preschool-age children have sleep-disordered breathing (Archbold et al., 2002; Redline et al., 1999). Identifying and treating sleep-disordered breathing may not only alleviate and improve the child's sleep but there is also evidence that sleep-disordered breathing is associated with a multitude of daytime problem behaviors (attention problems, anxiety/depression, hyperactivity, aggressiveness, and deficits in memory and language abilities) for preschool-age children (see Tauman & Gozal, 2011). Treatment of the sleep-disordered breathing may indirectly mitigate these behavioral correlates.

Although "behavioral insomnia of childhood" was defined in the second edition of the ICSD, this classification was eliminated in ICSD-3. Because it provides a useful means of discussing a particular group of extrinsic dyssomnias seen in childhood, however, we describe it here. Within "behavioral insomnia" are three types: association, limit-setting, and mixed (Cortese et al., 2014). "Sleep-onset association disorder" refers to the association of falling

asleep with exogenous cues (e.g., feeding, rocking, falling asleep with parent) and can lead to disorders of maintaining sleep, potentially later classified as "insomnia disorder." These problems tend to *decrease* with age (Cortese et al., 2014; Crowell, Keener, Ginsburg, & Anders, 1987). "Sleep fragmentation" (night waking) is one of the most common complaints of parents bringing their infant for well-baby visits. As noted in the description of normal sleep, most infants learn within the context of nighttime interactions with parents how to quiet themselves to sleep following night awakenings. A significant subset of infants, however, continues to have multiple and prolonged bouts of night waking that begin shortly after sleep onset and persist until morning rise time. For parents who view them as problematic, these awakenings may become a major source of family tension and be associated with significant parental conflict about managing the infant's sleep.

In contrast, the prevalence of limit-setting sleep disorder (typically occurring around bedtime) *increases* during the preschool period, which makes it a common problem in preschool-age children (Cortese et al., 2014; Crowell et al., 1987). "Limit setting" refers to the reinforcement of undesirable habits at wake-to-sleep transitions, and includes bedtime resistance and lengthy bedtime routines that delay sleep onset. Preschoolers, especially if there are older siblings in the family, enjoy participating in the family's evening activities. They fervently deny being tired when asked. Because daytime experiences for preschoolers are frequently exciting and overstimulating, calming down at bedtime may be difficult. Whatever the causes, the preschool child may protest vigorously, attempting to delay bedtime. Examples of protestation include requesting bedtime stories to be repeated, screen time to be extended, returning for more good night hugs and kisses, asking for another glass of water or snack, and pleading for "5 more minutes" until bedtime. A child may also insist on falling asleep in the parents' bed or while lying next to and holding the parents. These behaviors delay sleep onset and can considerably shorten total sleep duration (National Sleep Foundation, 2004).

Another category of sleep disorders that affects the preschool-age child is the "parasomnias," which are defined as episodic nocturnal behaviors that interrupt sleep but do not affect the architecture of the REM and NREM sleep cycles. They often involve cognitive disorientation, autonomic and skeletal muscle disturbances, and may be related to central nervous system immaturity (Mindell & Owens, 2003). NREM parasomnias appear to decrease with age, have a familial component, and occur at the transition out of deep sleep (NREM Stages 3–4). Night terrors are the most common parasomnia among preschool-age children who have high percentages of deep sleep. Any factor that increases the percentage of deep sleep (e.g., medications, sleep deprivation) has the potential to increase the frequency of these NREM parasomnia episodes (Klackenberg, 1982). Night terrors (an NREM parasomnia) should be distinguished from nightmares (an REM parasomnia), which can also become problematic in this age group. Dreams are normally reported by children after age 3 years (Foulkes, 1982), and nightmares shortly thereafter. Dream content

before children are age 8 years is usually short and concrete. Dream symbolization and elaboration are uncommon. Nightmares are anxiety dreams that awaken the sleeping child. Nightmares occur during REM sleep and result in a fully awake and oriented child who remembers and recounts the content of the dream. Young children who experience trauma may have intrusive nightmares as a symptom of posttraumatic stress disorder (PTSD; Scheeringa, Zeanah, & Cohen, 2011). Because REM sleep occurs most commonly in the latter third of the night, nightmares generally are noted in the early morning hours, after 2:00 A.M. in comparison to night terrors that occur in the beginning of the night and involve disorientation.

Impact on Daytime Functioning

Without effective interventions, both limit-setting and sleep-onset association disorders tend to persist (Meltzer & Mindell, 2014; Smedje, Broman, & Hetta, 2001, 2001b) and may lead to excessive daytime sleepiness and consequently impair daytime functioning. For example, Bruni, Lo Reto, Miano, and Ottaviano (2000) found that frequent nighttime awakenings were associated with higher Externalizing scale scores, and greater bedtime resistance was related to higher Internalizing scale and Total scale scores on the Child Behavior Checklist in preschool-age children. Thunstrom (2002) demonstrated that severe and chronic night waking during infancy was associated with an attention-deficit/hyperactivity disorder (ADHD) diagnosis at 5 years. Other studies support this association between early childhood sleep problems and later psychosocial disorders of regulation (Gregory, Eley, O'Connor, & Plomin, 2004; Lam, Hiscock, & Wake, 2003; Wolke, Rizzo, & Woods, 2002; Wong, Brower, Fitzgerald, & Zucker, 2004), although often these associations are accounted for by common psychosocial risk factors. More experimental studies are needed to confirm the existence and direction of these associations in preschool-age children; however, research is starting to emerge in this area (Berger, Miller, Seifer, Cares, & LeBourgeois, 2012).

There is a growing body of literature suggesting that sleep and cognitive functioning are related even in younger children. For example, Bernier, Carlson, Bordeleau, and Carrier (2010) found that toddlers with increasing sleep consolidation to the nighttime hours performed better on working memory and impulse control tasks at 18 and 26 months of age. Thorpe and colleagues (2015), however, report in their meta-analysis of studies on daytime sleep an approximately equal number of articles showing a cost to cognition as a benefit. It is likely that the developmental reduction in daytime sleep serves as a marker for neurocognitive development in general rather than suggesting that the reduction in sleep leads to better cognitive outcomes. This is supported by experimental research showing that restricting preschoolers' sleep by eliminating their daytime nap without a concurrent increase in nighttime sleep has a negative impact on children's emotional reactivity (Berger et al., 2012). When children do give up the daytime nap, their nighttime sleep

duration increases (Iwata, Iwata, Iemura, Iwasaki, & Matsuishi, 2012; Ward, Gay, Anders, Alkon, & Lee, 2008). It is likely that the final consolidation of sleep to the nighttime hours marks a significant developmental achievement, crowned by increased neurocognitive and socioemotional functioning. When nighttime sleep is disturbed, however, there is a concomitant daytime impairment in functioning. Evaluating the degree of a sleep disruption is therefore critical.

A DIAGNOSTIC CLASSIFICATION SYSTEM

The clinical diagnostic systems that are available currently are problematic for various reasons. The fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5; American Psychiatric Association, 2013) defines insomnia disorder as a group of disorders characterized by inadequate quantity or quality of sleep. However, young children do not typically meet the impairment and/or severity criteria. The ICSD-3 (American Academy of Sleep Medicine, 2014) removed the ICSD-2's inclusion of the category of "behavioral insomnia of childhood" in favor of a single umbrella diagnosis of "chronic insomnia disorder" (Meltzer & Mindell, 2014). These diagnoses use criteria that are vague and neither empirically nor developmentally determined. More importantly, pediatricians and professionals who work with preschool-age children may not be aware of the existence of the ICSD-3. The *Diagnostic Classification of Mental Health and Developmental Disorders of Infancy and Early Childhood—Revised* (DC:0–3R; Zero to Three, 2005) is yet another nosology, developed by early childhood specialists, that focuses on young children from birth to age 3 years. This diagnostic system takes a step forward in referring to subclassifications of sleep behavior disorders after 12 months of age. Importantly, none of these classification systems takes into account the context within which the child is developing (see Figure 10.1).

Therefore, we have proposed a different classification system that can be applied in both research and clinical settings to identify sleep problems in toddlers and preschool-age children. We have developed this classification system based on clinical experience and empirical data (Gaylor, Goodlin-Jones, & Anders, 2001; Gaylor, Burnham, Goodlin-Jones, & Anders, 2005). In addition, a simultaneous effort pushed for developmentally appropriate diagnostic criteria of psychopathology for preschool-age children, based on clinical evidence and considered useful for promoting research in clinical trials and epidemiological surveys (Scheeringa, 2003). This Task Force on Research Diagnostic Criteria for Infancy and Preschool (2003) has adopted our sleep disorders classification system for further testing (Anders & Dahl, 2007).

We have attempted to bridge the gap between research and clinical definitions of sleep disorders by developing acceptable and accurate research diagnostic criteria that can be ascertained by standard questionnaires and interviews

or by more objective measures, such as actigraphy or videosomnography. A classification system was needed that accounted for both normative sleep patterns and the caregiving diversity of contemporary society. We have described the classification system in detail elsewhere (Anders et al., 2000; Gaylor et al., 2001, 2005). In general, the system, as depicted in Table 10.1, describes two different disorders in young children: sleep onset (similar to limit-setting sleep disorder) and night waking (similar to sleep-onset association disorder). It is divided by severity criteria into three categories: perturbation, disturbance, and disorder, in an attempt to engage parents and professionals in determinations about when an intervention is necessary (Anders, 1989). This system addresses frequency and duration criteria and is culturally sensitive (e.g., it avoids using co-sleeping itself as a criterion for a sleep disorder, as previous criteria have done; cf. Richman, 1981). In previous iterations, the term "protodyssomnia" was chosen because the classification criteria were derived from the adult dyssomnia criteria for sleep disorders in DSM-IV. However, for simplicity sake, that term has been abandoned in this version. The scheme is developmentally sensitive by dividing the transitional period of early toddlerhood (12–23 months) from preschool-age children (24–48 months). Of note is the fact that this scheme does not classify a disorder before 1 year of age. There are certainly children with problematic sleep before that age; however, the relationship, family, and environmental contexts may require more attention than the infant's sleep problem during this age period (see Figure 10.1).

TABLE 10.1. Classification Scheme for Sleep Dyssomnias in Toddlers and Preschoolers

Sleep-onset dyssomnia (child must meet any two of the three criteria listed)	
12–24 months	(1) > 30 minutes to fall asleep; (2) parent remains in room for sleep onset; (3) more than three reunions.[a]
> 24 months	(1) > 20 minutes to fall asleep; (2) parent remains in room for sleep onset; (3) more than two reunions.
Night-waking dyssomnia	
12–24 months	One or more awakenings, totaling > 30 minutes.
> 24 months	One or more awakenings, totaling ≥ 20 minutes.
> 36 months	One or more awakenings, totaling ≥ 10 minutes

Note. A dyssomnia is not diagnosed before 1 year of age. The criteria pertain to solitary sleeping infants. Duration criteria might further be subdivided. Perturbations (one episode/week for at least 1 month) are considered variations within normal development. Disturbances (two to four episodes/week for at least 1 month) are considered as possible risk conditions that may be self-limiting. Disorders (five to seven episodes/week for at least 1 month) most likely are continuous and require intervention.

[a]Reunions reflect resistances in going to bed (e.g., repeated bids, protests, struggles).

[b]Awakenings must require parental intervention and occur after the child has been asleep for > 10 minutes.

Of course, it is important, especially at the younger ages, always to rule out other causes of sleep problems. For example, medical concerns must be excluded, such as middle ear infections, congestion, pain, or allergies. If any of these concerns is present, medical intervention and treatment must begin before treatment of the sleep disruption itself. Sometimes, however, after successful medical treatment, the sleep problem may continue due to the parent–infant interaction patterns that emerged in the middle of the night during the course of the acute illness.

BEST PRACTICES/TREATMENT

There are two primary settings in which a young child with a sleep disorder might come into contact with a clinician: a pediatric/family physician well-child visit (Chervin, Archbold, Panahi, & Pituch, 2001; Mindell, Moline, Zendell, Brown, & Fry, 1994) and a mental health clinic. Approximately 10–47% of parents of children presenting to a mental health clinic report that their child has symptoms of a sleep disturbance (Frankel, Boyum, & Harmon, 2004; Keren, Feldman, & Tyano, 2001). This symptom presentation translates into a diagnosis of a sleep disorder in 0–10% of patients attending infant mental health clinics (Emde & Wise, 2003) and up to 22% in community-based infant mental health clinics (Keren et al., 2001). Interestingly, the average age of the child at the time of evaluation in an "infant" mental health clinic is 31 months (Frankel et al., 2004). Although the pediatrician will have had numerous opportunities for prevention and intervention during the first 5 years of life, some parents and professionals rely on the "wait and see approach" with many early childhood problems. Therefore, because there is a stated reluctance to identify and label infants as sleep-disturbed, clinicians often first address disordered sleep during the preschool years.

In an attempt to study both the precursors of these problems and the sensitivity and specificity of our proposed classification system, we recorded the sleep patterns of 80 children, derived from a nonclinical, community sample, from 1 month to 1 year of age, using videosomnography. We then followed 68 of them annually until 4 years of age, using a structured parent phone interview. The videotapes were coded for specific sleep behaviors that are potentially predictive of problem sleep in toddlers and preschool children (e.g., non-self-quieting night awakenings, sleeping in close proximity to parents, requiring parental presence to fall asleep) (Gaylor et al., 2005). During the follow-up period, parent report of a sleep problem ranged from 7 to 18%. In contrast, the classification system found that 3 to 9% of children met criteria for a sleep-onset disorder or a night waking disorder at any given time between 2 and 4 years of age. The classification scheme demonstrated adequate sensitivity and specificity at 2 years, but sensitivity declined substantially at 3 and 4 years.

Another objective of this study was to examine the predictive validity

of early self-quieting patterns. Interestingly, we found that consistently non-self-quieting infants between 6 and 12 months of age (33% of the sample) were more likely to meet criteria for a sleep-onset disorder and to be co-sleeping at 2 years. Sleeping in the parents' room at 12 months of age was predictive of night waking at 2 years of age (although not meeting criteria for a night waking disorder). Approximately 25% of children were reported to be co-sleeping at each follow-up interview but only one-third of these parents reported this behavior to be problematic.

Most common sleep disturbances, including nightmares and bedtime protestations, are transient, ordinary occurrences that do not seriously disrupt family functioning. Table 10.1 provides a suggested set of criteria for distinguishing among mild perturbations, disturbances, and disorders that may be useful to clinicians. Additionally, sleep disorders can occur as part of a comorbid presentation of more general dysregulation. For example, children with autism tend to have higher rates of behavioral sleep disorders and circadian rhythm disorders (Krakowiak, Goodlin-Jones, Hertz-Picciotto, Croen, & Hansen, 2008). In treating sleep disorders, the clinician must be prepared to explore sources of anxiety and interventions that can address, as well as possible, the child's needs for comfort, security, regularity of sleep habits, and protection from overstimulation.

Taking a Sleep History

It is important not only to obtain a careful sleep history when evaluating children with sleep problems but also to inquire about sleep habits in all children with behavior problems. Some attention-deficit and hyperactivity symptoms may actually be manifestations of disordered sleep rather than actual syndromes (Owens, 2009); growth retardation also may be associated with sleep disorders (Stores & Wiggs, 1998).

A sleep history requires a detailed description of all sleep-related symptoms in the child and a thorough history of sleep problems and patterns in other family members. It is helpful to use the framework provided by the transactional model in gathering the data. There are four areas to focus on in the assessment: (1) The specifics of the sleep problem and for whom it is a problem; (2) infant characteristics, such as temperament or illness; (3) parent–child interaction patterns (sensitive, consistent, controlling); and (4) contextual factors, including both proximal factors (parental characteristics and family context) and more distal factors such as culture and environment (cf. Figure 10.1; Anders et al., 2000).

Other questions that need to be addressed include the following:

1. What is the age at onset of the problem?
2. What is the frequency of the symptom(s) in terms of events per week and per night, and what has been its course (stable, worsening, improving)?

3. What time during the night or day does the symptom occur, in terms of both clock time and time since falling asleep?

For example, parasomnias are related to sleep onset and not to clock time. They generally occur 90–120 minutes after falling asleep. Night terrors can be distinguished from nightmares in that the former occur during the first one-third of the sleep period in Stage 4 NREM sleep, and the latter occur later in the night, when REM sleep predominates.

The child's customary sleep habits, often referred to as "sleep hygiene," are important to understand. A list of suggested questions that clinicians may ask in order to get a better sense of a child's sleep hygiene is presented in Table 10.2. In addition to questions about the child's typical sleep–wake patterns, bedtime routines, and the like, clinicians should be sure to ask about the child's breathing during sleep, and the caregiver's perception of impacts on daytime behavior.

Monitoring Sleep and Waking Behavior

To obtain an adequate assessment of sleep patterns, a sleep diary or log should be completed for 1–2 weeks. The diary measures night-to-night stability of the problem(s) and includes information about sleeping, waking, and interactional behaviors. Structured questionnaires that identify sleep disorders and measure their severity are in short supply for this age group. Perhaps because preschool-age children fall somewhere between the still developing infant/toddler (2- to 3-year-olds) and the school-age child (6+ year olds), this group has largely been ignored. However, in order for early detection of sleep problems to occur, age-appropriate screening and surveillance of preschool-age populations is necessary. Screening tools for pediatricians are useful to detect severe problem sleep in a normative population (e.g., B = Bedtime Issues, E = Excessive Daytime Sleepiness, A = Night Awakenings, R = Regularity and Duration of Sleep, S = Snoring [BEARS]; Owens & Dalzell, 2005; Bruni et al., 1996; Chervin et al., 1997; Sadeh, 2004) and can help health practitioners who are in a position to identify sleep problems in children and implement education and intervention. The mental health clinician who is required to assess and treat multiple behavioral domains needs a well-validated measure to identify the impact of sleep disorders on behavior and functioning.

Screening Tools for Use in the Office

Parental report measures include the Child Sleep Habits Questionnaire (CSHQ; Owens, Spirito, & McGuinn, 2000) and the Pediatric Sleep Questionnaire (PSQ; Chervin, Hedger, Dillon, & Pituch, 2000), both of which are dimensional scales to evaluate problem sleep behaviors (bedtime problems, sleep-disordered breathing, etc.). These questionnaires have demonstrated reliability and validity with respect to identifying both behaviorally

TABLE 10.2. Suggested Sleep History Questions for Clinicians

1. What is the usual bedtime and rise time?
2. How regular are sleep habits?
3. What are the sleeping arrangements?
4. With whom does the child share a room or bed?
5. Do the child's symptoms disturb others?
6. Are bedtime rituals present?
7. How common are dreams and nightmares?
8. How common are night waking and bed-wetting?
9. In the absence of colds, is breathing labored?
10. Are pauses in breathing audible?
11. Is snoring prominent, regular?
12. Is mouth breathing common, regular?
13. Is the child sleepy during the day, or is the child alert and active?
14. Does the child nap regularly?
15. Do the nighttime symptoms encroach on normal social functions? For example, is the child embarrassed to sleep at a friend's house or away at camp because of the sleep problem?
16. Does a child's sleep schedule fit well with the family's schedule in a socially appropriate way, and is the child's need for sleep met by the current schedule?
17. What type of interaction is typical at bedtime and naptime?
18. How long does it take the child to fall asleep once in his or her sleeping place?
19. Does he or she fall asleep alone or with others?
20. Does he or she waken during the night and cry out for someone? How many times during the night, and how many nights during the week? Who usually responds? How long does it take the child to return to sleep? What soothing techniques are required?
21. What sleep aids does the child use?
22. What are middle-of-the-night interactions like?

and medically based sleep disorders in children ages 2–8 years (Chervin et al., 2000) and 4–10 years (Owens et al., 2000). The CHSQ has been adapted for use in parental interviews in a younger population (age 1–4 years) by the authors (Gaylor et al., 2001, 2005), although psychometric data from the interview format have not been calculated.

Laboratory Assessments

Laboratory methods are indicated if the problem is believed to be an intrinsic dyssomnia, if parental report is suspect, or if excessive daytime sleepiness is evident (Carroll & Loughlin, 1995). Polysomnography (PSG), a diagnostic tool that examines sleep architecture and shows details about breathing, movement, and arousals during sleep, is usually indicated to diagnose

sleep-disordered breathing, periodic leg movement, and/or unexplained excessive daytime sleepiness. For example, Gozal and colleagues (O'Brien et al., 2004; Tauman, O'Brien, Holbrook, & Gozal, 2004) used a sleep pressure score derived from PSG to demonstrate that the severity of sleep-disordered breathing differentially predicts the level of daytime sleepiness and problem behavior in children ages 1–18 years. However, PSG studies are expensive and not always covered by insurance, especially for young children, nor are they always necessary.

Promoting Sleep Hygiene and Treating Disorders

A specific treatment depends on a clear diagnosis. For example, a diagnosis of obstructive sleep apnea syndrome in this age group is most often relieved by a tonsillectomy and adenoidectomy (Marcus et al., 2013). Similarly, a night terror disorder is best treated by parental reassurance and support. With maturation of sleep patterns, most parasomnias disappear spontaneously. However, for the more common night waking and sleep-onset dyssomnias, a number of general behavioral strategies to assist families have been advised. These range from letting the child cry in his or her own sleep environment for 5–7 nights to withdrawing parental presence gradually by waiting a longer time before intervening (Ferber, 1985), to shaping sleep hygiene behaviors (Meltzer & Mindell, 2014). Although there is certainly clinical support for using such techniques, and there is some empirical evidence pointing to their potential efficacy (Mindell et al., 2006), behavioral strategies are not universally found to be efficacious for all children, and parents report mixed success (Loutzenhiser, Hoffman, & Beatch, 2014). From the perspective of the transactional model, interventions should be more relationship-based and focused on the factors that impact optimal parent–child regulation; that is, each intervention should be individualized to the particular child and family, and consider the context within which the family exists.

The impact of parent–child interaction as a critical "regulator" of sleep–wake transitions and the process of consolidation is clear. It is one of the most consistent findings for factors influencing sleep problems in early childhood (Anders, 1994; Ferber & Kryger, 1995; Goodlin-Jones et al., 2000; Teti et al., 2010; Tikotzky & Sadeh, 2009; Ware & Orr, 1992). The manner in which the parent conducts the bedtime routine influences how the child settles at the beginning of the night and his or her behavior after a nighttime awakening. A typical pattern of back rubbing or rocking a child to sleep at sleep onset is then expected again in the middle of the night if the child wakens (Adair, Bauchner, Philipp, Levenson, & Zuckerman, 1991; Anders et al., 1992). Mothers who were rated as inconsistent in their handling of the infant at bedtime and fluctuated between different styles of interaction had infants who exhibited delays in falling asleep (Scher & Blumberg, 1999). According to the American Academy of Pediatrics, it is best to place the child drowsy but awake in his or her own bed at the beginning of the night (Cohen,

1999). Children supposedly develop a "positive sleep association" when they make the mental association between lying quietly in their bed by themselves and falling asleep. Parental presence at the beginning of the night also may discourage the use of a sleep aid by the child (Wolf & Lozoff, 1989). Three-month-old and 8-month-old infants who used a sleep aid were more likely to be placed in their bed awake and to use a sleep aid to self-soothe in the middle of the night (Anders et al., 1992). Last, the absence of a regular bedtime routine is associated with sleep problems (Cohen, 1999; Quine, Wade, & Hargreaves, 1991).

Given these data, it seems apparent that good sleep hygiene begins early in the infant's life and the use of potentially "preventive" parenting practices around sleep may be useful. We have learned that there are significant differences in the way parents of 9- to 12-month-old night-waking infants who do not self-quiet handle their infants at bedtime by 4 months of age. In general, after 4 months of age, parents of non-self-quieting infants place their infants into the crib when they are already asleep. Infants who were able to self-quiet after a nighttime awakening were more likely to have been placed into their crib while awake from as early as 4 months of age, and allowed to fall asleep on their own at the beginning of the night. Prior to 4 months of age, almost all infants fall asleep while feeding and are put into their cribs already asleep. But by 4 months of age, the transition to wakeful sleep onsets in the crib has begun (Burnham et al., 2002).

In addition, self-quieting infants are more likely to make use of a sleep aid, such as a pacifier, to help them fall asleep on their own. Non-self-quieting infants, in contrast, do not avail themselves or have access to a sleep aid, because they are already asleep. In the middle of the night, after an awakening, the process of falling asleep is repeated. Self-quieting infants, when they awaken for 3–5 minutes, fall asleep on their own; they frequently use their sleep aid. Non-self-quieting infants awaken, become fussy, and begin to cry. They seem to use their parents as their sleep aid (Anders et al., 1992).

From these observations, it appears that "preventive" sleep hygiene strategies should encourage infants to "learn" to fall asleep on their own after 4 months of age; that is, after 4 months of age, parents who want to encourage self-quieting should engage their babies in wakeful activity following a feeding for a few minutes, before putting them into their cribs while they are still awake. Letting the baby fall asleep by him- or herself at the beginning of the night will enhance the likelihood of a repetition of that pattern following a nighttime awakening after 4 months of age. Parents might also encourage the use of a sleep aid, such as a pacifier, thumb, or soft object, when falling asleep. Finally, additional advice might include moving the infant's crib out of the parental bedroom after 6 months of age. All of these suggestions, however, must be offered in the context of the family's values and beliefs, and the child's own characteristics and temperament. Concurrence between both parents (where applicable) with any advice is essential. If these preventive measures are followed consistently, night waking that is viewed as problematic by

parents should be minimized. One important caveat is that nursing infants often require additional nighttime feedings so some waking is expected after sleep onset.

But what to do with 2-year-old James described at the beginning of this chapter, whose nighttime awakenings have totally disrupted his family? A careful history and 2-week sleep diary revealed that James was not really sleep deprived, because he obtained most of his sleep napping during the day. It was his parents who were severely sleep deprived. James had not made the diurnal transition to consolidating daytime waking and nighttime sleep. Intervention in this case involved educating the parents about the importance of regular schedules; darkening the environment at night; establishing nighttime bedtime routines; and providing a calm, customary sleep environment for the child. A shaping protocol was instituted that shortened James's daytime naps gradually over a 2-week period. Day–night sleep diaries were closely monitored, and daily phone calls with the mother provided encouragement and support. The father, who was the primary daytime caregiver, was encouraged to sleep whenever the toddler slept and, for the duration of treatment, the mother was encouraged to sleep in a separate room, so that she could get enough sleep to function at work. James's crib was moved into his father's room, and when he awakened at night, his father talked softly to him and rubbed his back, without feeding him or taking him out of his bed. Over a 2-week period, James shifted his diurnal sleep–wake rhythm and became much easier to calm. When he became a self-quieting infant in his father's room, his crib was returned to his own room, and his father slept on a bed next to his crib. He gradually moved further away, until James was able to self-quiet in his own room. James's mother and father were then reunited in their room, and family harmony was restored. Within the month, James was taking one afternoon nap and slept alone in his own room at night.

FUTURE DIRECTIONS

We clearly need more information about sleep disorders in preschool-age children in clinical settings (Frankel et al., 2004; Dunitz, Scheer, Kvas, & Macari, 1996; Keren et al., 2001). Cultural changes in the demands on parents (e.g., increase in dual-working-parent households, use of child care) may affect the child's presentation and the parents' tolerance of certain behaviors (e.g., sleep symptoms, separation anxiety). Oftentimes, studies do not include a representative sample or sufficient description of ethnic and cultural characteristics. We need more information about the effects and consequences of sleep loss for cognitive, learning/memory, behavioral, and psychosocial development. And finally, we need more information about how relationship patterns, as influenced by the factors that comprise the transactional model, affect sleep–wake state organization and the emergence of sleep problems in this age group. Clearly, there is plenty of additional research needed on sleep and its

development and disorders in early childhood. Clinicians should direct a keen eye toward the research literature, as this research will be informative to practice. In the meantime, effective clinicians will continue to ask questions about sleep habits, environments, and issues in an effort to obtain a comprehensive understanding of the child's sleep in the family context.

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Part III

Empirically Supported Interventions for Disorders in Preschool Children

11

Parent–Child Interaction Therapy and Its Adaptations

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"Disruptive behavior disorders" (DBDs), which refers to serious and impairing problems of conduct or oppositionality, are highly prevalent in childhood (e.g., Costello, Mustillo, Erkanli, Keeler, & Angold, 2003; Egger & Angold, 2006), with estimates indicating that 1 in 11 preschoolers meets diagnostic criteria for a DBD (Egger & Angold, 2006). Untreated DBDs are associated with a host of negative sequelae, including comorbid psychological illness, family dysfunction, antisocial behavior, substance abuse, and criminality (e.g., Broidy et al., 2003; Gau et al., 2007). Early intervention is critical.

Psychosocial treatment—in particular, behavioral parent training programs—has received robust support as a first-line intervention for early disruptive behavior problems (Comer, Chow, Chan, Cooper-Vince, & Wilson, 2012), particularly those programs that increase parent–child interactions, teach parents to use time-out and to parent consistently, and require parents to practice new skills with their children during treatment sessions (Kaminski, Valle, Filene, & Boyle, 2008). Parent–child interaction therapy (PCIT; Eyberg & Funderburk, 2011; McNeil & Hembree-Kigin, 2010) is among the best supported of such interventions. Informed by attachment and social learning theories, as well as by developmental science, PCIT targets DBDs in children ages 2–7 by intervening in the parent–child relationship. Therapeutic gains are achieved by teaching parents authoritative parenting techniques to foster warmth and positive attention, clear communication, and effective discipline

strategies. PCIT is distinguished from neighboring behavioral parent training approaches by its use of live, directive parent coaching via a bug-in-the-ear device; during treatment sessions, the therapist observes parent–child interactions from behind a one-way mirror, unobtrusively providing parents with real-time coaching of treatment-specific skills. PCIT is a mastery-based intervention, with treatment termination determined by (1) parents' mastery of treatment-specific skills defined by prespecified criteria, and (2) reduction of child behavioral problems to subclinical levels.

PCIT is structured in two phases. The first phase of treatment, child-directed interaction (CDI), aims to increase warmth and positivity within the parent–child relationship and improve the child's behavior through the use of differential attention. Because the parent–child relationship is often strained for children with DBDs, improving the positivity within the parent–child relationship is prioritized first, so that these interactions become more reinforcing for the parent and the child, who is subsequently more likely to accept parental limits (Eyberg & Funderbunk, 2011). During CDI, parents follow their child's lead and shape appropriate child behavior by increasing attention to desired child behaviors and minimizing response to problematic ones. Parents are instructed in the "Do" skills, summarized by the PRIDE acronym: ***P****raise* (specific verbal praise of desired behavior); ***R****eflection* (repeat appropriate child verbalizations); ***I****mitation* (copy appropriate behavior); ***D****escription* (narrate the child's appropriate behavior as it occurs); and ***E****nthusiasm* (express verbal and nonverbal interest in the child's behavior). Parents are also discouraged from using three specific "Don't" behaviors during CDI—asking *questions*, giving *commands*, and *criticizing* the child—because these parent behaviors often provoke conflict within the parent–child interaction.

CDI begins with a parent-only "Teach" session, during which the therapist instructs parents in these "Do" skills and "Don't" behaviors. Subsequent CDI sessions are "Coach" sessions, during which parents practice applying these skills while following their child's lead while he or she directs the play. The therapist observes the parent–child interaction during Coach sessions from behind the one-way mirror, coding parents' competence in the use of CDI skills and providing coaching via the bug-in-the-ear device. Practice between sessions is crucial, and parents are assigned to practice CDI skills with their child for 5 minutes every day. At the beginning of each CDI session, the therapist assesses the child's behavior problems from the past week and evaluates parents' progress in mastering CDI skills during a 5-minute coded parent–child interaction task. For each session, the real-time CDI coaching, which takes up the bulk of each session, is directly informed by the parents' performance during this structured interaction task. CDI Coach sessions continue until parents demonstrate formal mastery of the CDI skills, as evidenced by standardized criteria: Within a 5-minute coding period, the parent expresses at least 10 praises, 10 reflections, and 10 descriptions, with three or fewer total Questions, Commands, or Criticisms.

After parents meet CDI mastery, treatment transitions to its second phase:

parent-directed interaction (PDI). During PDI, parents are taught to improve their limit setting through the consistent use of an effective discipline strategy. PDI emphasizes the use of direct commands, which are specific, clear, and positively stated (i.e., "Please hand me the block"), as opposed to indirect commands (i.e., "It would be great if you gave me that block"), to foster clear communication. PDI makes use of a time-out chair, to which the child is sent for noncompliance for 3 minutes (plus 5 seconds of quiet). However, if the child does not stay on the time-out chair as instructed, the parent takes the child to a time-out backup room for 1 minute (plus 5 seconds of quiet). This structured and consistent procedure helps children quickly learn that getting out of the chair without permission only prolongs their consequence, because they must return to the time-out chair after being in the time-out backup room. After the child successfully stays in the time-out chair, he or she must then comply with the initial command that he or she disobeyed. If the child again does not comply, the time-out sequence is again initiated.

Time-out rooms in the clinic are typically small, well-lit, empty rooms that provide a safe and contained space. These rooms prevent children from receiving attention or reinforcement from fun activities after getting off of the time-out chair without permission. When implemented properly, typically the time-out backup room is only needed a handful of times before the time-out chair itself suffices. Therapists problem-solve with parents to identify an appropriate time-out backup room in their home that serves the same functions, while maintaining the child's safety.

As with CDI, PDI begins with a parent-only Teach session, during which effective commands are explained and the PDI time-out procedure is introduced and taught. The PDI procedure provides parents with both precise language to communicate neutrally to the child during the time-out procedure and established durations for the child to remain in the time-out chair or the time-out backup room. Absolute fidelity to the procedure and consistency in implementation is critical in order to ensure predictability and consistency in parental discipline. Parents introduce PDI to the child during the first PDI Coach session, during which the therapist actively coaches them through the time-out procedure to ensure that parents learn how to follow PDI precisely. Subsequent PDI Coach sessions focus on coaching parents, via the bug-in-the-ear device, in the continued use of CDI skills from behind the one-way mirror, while also promoting the effective use of direct commands and follow-through in the PDI time-out procedure in response to disobedience. As in CDI, home practice is essential during the PDI treatment phase, and parents are expected to practice both CDI and PDI daily.

Empirical work strongly supports the efficacy of PCIT, demonstrating that the intervention is associated with significant improvement in both the child's behaviors and parents' practices, parental confidence, and reduced parental depression (e.g., Eyberg, Boggs, & Algina, 1995; Eyberg et al., 2001; Schuhmann, Foote, Eyberg, Boggs, & Algina, 1998; Thomas & Zimmer-Gembeck, 2007; see Zisser & Eyberg, 2010, for a summary). For example, results of an

open trial of PCIT indicated that 11 out of 13 (92%) children no longer met diagnostic criteria for a DBD at posttreatment (Eyberg et al., 2001). Similarly, results of a randomized controlled trial (RCT) examining the efficacy of PCIT for the treatment of 3- to 6-year-old children with DBDs indicated that child disruptive behaviors decreased to subclinical levels for the immediate treatment group (n = 37) but remained unchanged for the control group (n = 27; Schuhmann et al., 1998). Evidence suggests that treatment effects of PCIT are maintained well beyond treatment termination, with long-term maintenance effects demonstrated for up to 6 years posttreatment (Hood & Eyberg, 2003), and PCIT has been shown to be effective in the treatment of children from diverse socioeconomic, cultural, and language backgrounds (Funderburk & Eyberg, 2011; Zisser & Eyberg, 2010). PCIT is a well-established evidence-based treatment and in 2009 was added to the National Registry of Evidence-Based Programs and Practices (NREPP; *www.nrepp.samhsa.gov*).

ADAPTABILITY OF PCIT

Treatment developers have increasingly recognized the clinical benefits that this unique PCIT format and approach affords for the treatment of young children, and compelling new research has extended the range of treatment targets, ages, and settings in which PCIT-related adaptations and modifications may be applied. Although these diverse treatment targets and populations vary widely, there exists a strong rationale for applying PCIT-related approaches to these populations over other treatment approaches (see Carpenter, Puliafico, Kurtz, Pincus, & Comer, 2014). First, although a range of empirically supported interventions have been developed for internalizing problems in school-age children and adolescents, there has historically been a relative lack of empirically supported interventions specifically designed for preschoolers (see Luby, 2013; Mian, 2014; Puliafico, Comer, & Pincus, 2012). Whereas the interventions for internalizing problems in older children that have received considerable support draw heavily on cognitive strategies that may be beyond the developmental capacities of younger children, adaptations of PCIT—which do not target children directly, but rather work to reshape the primary context of child development—can offer more developmentally compatible approaches for intervening with internalizing preschoolers. Second, parents can often be inadvertently involved in the development and/or maintenance of a range of early child symptoms (not just externalizing problems), so modifying parental responses can be even more critical for effective treatment in younger populations. Behavioral parent training approaches are well suited to achieve this goal, and the unique PCIT format affords the in-session practice and real-time coaching that can lead to greater gains and generalizability of outcomes. Third, comorbid internalizing and externalizing conditions are highly prevalent in preschool populations (Egger & Angold, 2006); in fact, researchers suggest that co-occurring behavior problems may lead parents to

seek services for anxiety (Mian, 2014; Mian, Godoy, Eisenhower, Heberle, & Carter, 2016). Therefore, families seeking services to manage internalizing conditions may also benefit from treatment approaches such as PCIT that also address externalizing behaviors. CDI skills may even be effective in addressing parenting styles linked to internalizing symptoms, in addition to those associated with externalizing problems (Chase & Eyberg, 2008). Finally, in the case of anxiety disorders, PCIT's live coaching format may be ideal for supporting parents' ability to tolerate distress in the context of challenging child behavior, whether it be internalizing or externalizing concerns.

In the sections that follow, we introduce supported adaptations, modifications, and extended applications of PCIT for early childhood mental health problems and outline burgeoning areas of research and clinical study. Specifically, we focus on (1) PCIT for separation anxiety disorder; (2) the PCIT-CALM program for the range of early anxiety disorders; (3) the Turtle Program, targeting behavioral inhibition in young children; (4) PCIT-ED for early childhood depression; (5) PCIT for young children with developmental delay; and (6) PCIT for at-risk infants.

SUPPORTED ADAPTATIONS, MODIFICATIONS, AND EXTENDED APPLICATIONS

PCIT for Separation Anxiety Disorder

Separation anxiety disorder (SAD), characterized by persistent and excessive fears of separation from caregivers, is one of earliest anxiety disorders with a childhood onset. While some separation anxiety is a developmentally normal part of infancy and early childhood, approximately 4–8% of youth show impairing difficulty in navigating separation situations (Bufferd, Dougherty, Carlson, Rose, & Klein, 2012; Egger & Angold, 2006). Parents of children with SAD often display myriad behaviors in an attempt to cope with their child's distressing pleas, such as providing excessive reassurance or permitting the child to avoid separation situations. Although these behaviors may reduce children's distress in the short term, these parental accommodation behaviors can inadvertently exacerbate separation anxiety symptoms by restricting the child's developmentally appropriate autonomy and reinforcing maladaptive behaviors and avoidance (Lebowitz et al., 2013; McLeod, Wood, & Weisz, 2007; Thompson-Hollands, Kerns, Pincus, & Comer, 2014). Aversive parent–child interactions often ensue when parents do not accommodate children's separation concerns, or when daily demands and schedules require more expedient separation (Carpenter et al., 2014).

Given the maladaptive parent–child interactions that can result in anticipation of and during separation situations, a parenting-based treatment approach such as PCIT is likely to be particularly useful for families with young children with SAD (Pincus, Santucci, Ehrenreich, & Eyberg, 2008; Puliafico, Comer, & Albano, 2013). Parents of youth with SAD may also

benefit from becoming aware of the parenting behaviors that may maintain child anxiety, including excessive reassurance, overprotection, and facilitation of avoidance (Hudson, Comer, & Kendall, 2008; McLeod et al., 2007; Waters, Zimmer-Gembeck, & Farrell, 2012). Parents of young children with SAD can benefit from learning to modify their parenting styles and behaviors in order to decrease their child's separation symptoms, to use skills such as labeled praise to reinforce children's nonavoidant and brave behaviors, and to encourage approach of developmentally appropriate situations. Furthermore, a parenting-based treatment approach can help teach parents skills for coping effectively with their child's anxiety-related tantrums when they occur, including learning skills to implement time-out procedures appropriately when they are necessary. Thus, a PCIT-based approach to treating SAD can provide parents with tools to cope more effectively with child behavior, including separation anxious behavior, so that negative parent–child interaction patterns associated with separation and its avoidance can be meaningfully reduced.

Pincus and colleagues were the first to examine whether PCIT-based approach could redress the problems of children with SAD (Choate, Pincus, Eyberg, & Barlow, 2005; Pincus, Eyberg, & Choate, 2005; Pincus et al., 2008, 2010). In their first study on the topic (Choate et al., 2005; Pincus et al., 2005), a multiple-baseline open trial (n = 3) was employed to test whether PCIT in its standard form could reduce symptoms of SAD in young children. All three children experienced reductions in SAD symptoms and disruptive behaviors, but in a larger, open trial using standard PCIT to treat 10 children with SAD (Pincus et al., 2008), none of the participants showed clinically significant reductions in symptoms; although separation anxiety improved, all met diagnostic criteria for SAD at posttreatment. Many parents reported that they still needed assistance in knowing how to help children begin to approach previously avoided separation situations. Thus, while standard PCIT was helpful, it seemed insufficient to fully meet the needs of youth with SAD.

Pincus and colleagues then developed an additional treatment phase to teach parents how to promote children's "approach" behaviors. In this modified PCIT program, a three-session, anxiety-focused treatment module called "bravery-directed interaction" (BDI) was developed and inserted between abbreviated three-session formats of CDI and PDI. Thus, the resulting protocol included three, fixed-length (3 sessions) phases: CDI, BDI, and PDI. CDI and PDI are conducted with the traditional PCIT live coaching (parents wore a bug in the ear), and session content is from traditional PCIT. In the BDI phase, an initial Teach session provides parents with education regarding the cycle of anxiety and factors that can maintain separation anxiety behaviors. Parents are taught how to conduct graded exposures effectively with their child during the second and third sessions, during which planned "exposure" to anxiety-provoking situations is attempted gradually, and a "bravery ladder" (e.g., hierarchy of feared separation situations) is collaboratively created with the child and parent. These feared separation situations are listed in order from least anxiety provoking (e.g., going to a daytime birthday party without a parent) to most anxiety provoking (e.g., going to a sleepover without a

parent). In this particular PCIT modification for SAD, the actual exposures occur largely outside of session. Parents are also provided with a list of "Do" skills and "Don't" behaviors to guide them in how to help their child approach previously avoided separation situations effectively.

The preliminary efficacy of PCIT for SAD was evaluated in an RCT conducted with 38 children ages 4–8 with SAD (Pincus et al., 2010; Pincus, Chase, Hardway, Comer, & Eyberg, 2016), comparing families receiving immediate PCIT for SAD to a waitlist control condition. Initial results indicated that at posttreatment, 73% of children receiving PCIT for SAD no longer met criteria for a diagnosis of SAD; these results are contrasted with youth who received the waitlist condition—at posttreatment, 0% of participants in the waitlist were diagnosis free. Improvements seen in those who received this modified PCIT were maintained at 3-month follow-up. Children showed reductions in their avoidance of previously feared situations, and parents reported significant decreases in parenting stress. This program of research suggests that in addition to the essential parenting skills taught in traditional PCIT, parents of youth with anxiety may benefit from an additional exposure-based component.

PCIT-CALM Program for the Range of Anxiety Disorders in Early Childhood

Building on the preliminary success of Pincus and colleagues' modified PCIT for SAD, Comer and Puliafico developed the Coaching Approach Behavior and Leading by Modeling (CALM) program (Puliafico et al., 2013) to address the full range of anxiety disorders that present in early childhood. This program expanded upon the modified PCIT for SAD protocol in several important ways. First, the CALM program targets a wider age range of young children (ages 3–8 years) presenting with a broader range of anxiety disorders (SAD, social anxiety disorder, generalized anxiety disorder, and/or specific phobias). Second, the CALM protocol places greater emphasis on in-session, parent-led exposures and parental modeling, while incorporating live bug-in-the-ear parent coaching during *in vivo* exposure tasks. Third, the CALM program includes six CDI sessions instead of just the three included in PCIT for SAD. Fourth, the exposure-based module of CALM is eight sessions long, with real-time coaching in low-level exposures occurring prior to real-time coaching of parents in higher-level exposure-based tasks. Finally, the CALM protocol does not include PDI, because many parents of young children with anxiety disorders do not need to focus on improving effective discipline. In contrast to PCIT for SAD, in the CALM program, therapists provide live coaching of parent-led exposures in session, allowing parents to benefit from therapist guidance as they help their child navigate anxiety-provoking situations. As in PCIT for SAD, parents and children in the CALM program develop a "fear ladder" in which feared situations are organized in order of least to most anxiety provoking, and parents are coached to lead children in exposure tasks while encouraging brave behavior.

The CALM program is designed to teach parents particular steps to encourage and reinforce children's brave behavior during exposure exercises, referred to as the "DADS" steps: (1) **D**escribe the situation (e.g., "I see a large dog over there"), (2) **A**pproach the situation first themselves (e.g., the parent goes over and pets the dog), (3) give a **D**irect command for the child to join the situation (e.g., "Billy, please take one step toward the dog"), and (4) provide **S**elective attention based on the child's performance, either praising approach behavior or ignoring anxious behaviors (e.g., "I love how you took a step closer to the dog" vs. active ignoring while the parent continues to pet the dog). The CALM program allows therapists to shape parents' and children's behavior in real time, while also enabling parents to continue to foster children's bravery by practicing out-of-session exposures between sessions and after treatment is completed.

In a preliminary test of the efficacy of the CALM program, Comer, Puliafico, and colleagues (2012) conducted a multiple-baseline evaluation for anxious youth between ages 3 and 8 years, presenting with a range of child anxiety disorders. A sample of nine anxious youth completed 12 weekly, 60-minute sessions of the CALM protocol. Following completion of the CALM protocol, 86% of treatment completers no longer met diagnostic criteria for an anxiety disorder, and all children demonstrated significant reductions in global impairment.

The CALM protocol was designed to maximize sessions in which families could engage in exposure-based tasks; thus, the teaching and coaching of PDI was not included. However, given that earlier modifications of PCIT by Pincus and colleagues (2005) for SAD did include PDI sessions, it is still unclear how relevant this component is for children with internalizing problems. Work is currently under way to develop a treatment program that integrates the strengths of the PCIT for SAD program and the CALM program, which is being referred to as the PCIT-CALM program. The PCIT-CALM program incorporates the DADS steps into an expanded BDI module that allows time for in-session exposures and real-time coaching. Furthermore, efforts are currently under way to develop a modularized PCIT program for the treatment of early preschool psychopathology, such that after a thorough assessment of the child and families presenting problems, the PDI component could be introduced to families when a child's disruptive behavior co-occurs with anxiety problems, along with the BDI and CDI components. Overall, these programs hold tremendous promise for treating the range of early anxiety problems in young children, and for helping parents develop skills to facilitate children's continued success.

The Turtle Program

Another recent adaptation of PCIT targets behavioral inhibition in preschool-age children. Estimates indicate that 15–20% of young children can be classified as behaviorally inhibited (BI), a temperamental style characterized by

wariness and withdrawal from unfamiliar situations or people (Degnan & Fox, 2007; Rubin, Coplan, & Bowker, 2009). Prospective studies demonstrate that BI is often a stable trait that persists across development, and that the emergence of BI in early childhood predicts the development of anxiety disorders by adolescence (Chronis-Tuscano et al., 2009). Moreover, empirical work has uncovered strong associations between childhood BI and parenting styles characterized by high degrees of intrusiveness, overprotection, overcontrol, and inappropriate warmth (Rubin, Burgess, & Hastings, 2002). Transactional models of BI propose that parents often excessively accommodate or overmanage their child, such that he or she fails to learn coping strategies, which contributes to the development of anxiety disorders (Rubin et al., 2009). The well-documented associations between BI and insecure parenting styles, coupled with the negative sequelae of early childhood BI, highlight the need for early intervention.

Given the primacy of parent–child interactions and their links with BI and associated conditions, Chronis-Tuscano and colleagues (2015) developed an adaptation of PCIT to provide an early intervention program for preschoolers with BI, the efficacy of which has recently been evaluated through an RCT. The Turtle Program, so named because it aims to help children "come out of their shells," is designed for delivery in a group format, during which five to six parent–child dyads meet for eight weekly sessions, with parents and children meeting in separate groups. Similar to the model developed by Pincus and colleagues (2005) described earlier, the parent component of the treatment is delivered through three modules: CDI, BDI, and PDI. In CDI, parental reinforcement of their child's independent behaviors or appropriate social interactions is introduced, and emphasized throughout the program. During BDI, parents are coached to engage their child in anxiety-provoking situations, pairing reinforcement for social approach behaviors with active ignoring of clingy or avoidant behaviors. Parents are taught to differentiate between anxious behavior and oppositional behavior, and during PDI learn effective discipline strategies to address oppositional behavior when appropriate. As with traditional PCIT, the therapist provides live, unobtrusive coaching of the parent–child interaction from behind a one-way mirror. Other parents in treatment observe the coaching from another room via television to allow for modeling and vicarious learning. Children in the Turtle Program receive social skills training in a group format, adapted from the Social Skills and Facilitated Play program (Coplan & Schneider, 2005), to reinforce appropriate social interactions and problem solving, while also teaching coping and relaxation strategies. Multi-informant results from the RCT provide compelling preliminary support for this intervention (see Chronis-Tuscano et al., 2015). Compared to a waitlist control group, at posttreatment, children in the Turtle Program demonstrated significant improvements in BI, social anxiety symptoms, and internalizing problems according to parent report, and observational data revealed increases in maternal positive affect/sensitivity. Teacher-report measures similarly indicated significant decreases in child anxiety

symptoms for children in the active treatment group, providing initial support for cross-situational utility of the Turtle Program. Follow-up investigations and mediator–moderator analyses are needed, but this preliminary work provides encouraging support for the efficacy of the Turtle Program to address early childhood BI.

PCIT–Emotion Development

PCIT–emotion development (PCIT-ED) was developed by Luby and colleagues for the treatment of preschool-onset depression (Luby, Lenze, & Tillman, 2012; Stalets, Pautsch, McGrath, & Luby, 2014). PCIT-ED includes three modules: CDI and PDI (both limited to six sessions each) and a novel ED module. The ED module was initially designed and tested as a six-session module but has been increased to eight sessions in more recent adaptations (Stalets et al., 2014). The ED module builds on skills learned in CDI and PDI but differs from traditional PCIT in that, in addition to parent coaching, it involves direct teaching of emotional competence to the child (Stalets et al., 2014). ED sessions include "Teach" sessions that focus on parents' own style of emotional expression, the child's pattern of emotional reactivity, and the parents' role as a "regulator," and "guide" for the child's emotional development. Parents practice applying knowledge of emotional expression using a videotaped example (from a previous session) of the child's emotional reaction. Parents are taught the Support Steps, which are done in the moment when the child is upset and include preparing to help the child, observing the emotion source (i.e., the triggering event) and the child's reaction, connecting the emotion and emotion source, calming oneself, working together to develop solutions to the problem, and reassuring (validating that the feeling is OK and that the parent is not mad at the child). Parents are then taught the GUIDE steps: ***G****o* back and state the source of the emotion, state your **U**nderstanding of the child's emotion, state the ***I****deas* and thoughts the child might have had about the emotion source, ***D****escribe* what was true and untrue about the event, and ***E****xpress* affection and confidence. The GUIDE steps are to be implemented after an emotional reaction to prepare the child for future episodes.

The child is then directly taught about different feelings in an interactive manner (e.g., discussing pictures taken of the child expressing different emotions; identifying emotions in story characters). Children are taught to use diaphragmatic breathing as a relaxation tool, and to identify a "relaxation station," which is a specific place in the home to go when having intense emotions (note this is *not* a time-out location, because it is not to be used for punishment). Once the basic skills have been introduced, parents are coached using the bug-in-the-ear technique to apply the support and GUIDE steps while the child engages in various activities designed to elicit difficult emotions (e.g., anger/frustration, guilt). As with traditional PCIT, all ED skills are practiced at home and coded in session. Parents are also taught how to enhance CDI skills to promote increased positive affect during activities with parents.

PCIT-ED has received initial empirical support, demonstrating significantly more symptom improvement compared to a psychoeducation control in a small (n = 29 completers), pilot RCT with depressed preschool-age children (Luby et al., 2012). While both groups demonstrated improvements, intent-to-treat analyses indicated that the PCIT-ED group evidenced significant improvement across a wider range of constructs, including depressive symptoms, externalizing symptoms, functional impairment, emotion regulation, and parent stress. To build on these encouraging results, Luby and colleagues are currently running a larger RCT to further investigate the efficacy of PCIT-ED with 250 depressed preschoolers (Joan Luby, personal communication, June 2, 2015).

PCIT for Young Children with Developmental Delay

Bagner and colleagues have worked to examine the utility of PCIT when applied to treatment of behavior problems in children with developmental delay. In an initial randomized trial of youth with intellectual impairment (i.e., IQ range: 55–75; n = 30), Bagner and Eyberg (2007) found that standard PCIT resulted in fewer behavior problems, more child compliance, reduced parent stress, and more positive parent–child interactions in youth with intellectual impairment than in a waitlist control condition. Building on this work, they examined the efficacy of PCIT for the treatment of behavior problems in young children born prematurely (i.e., < 37 weeks gestation) in a waitlist controlled trial (n = 28; Bagner, Sheinkopf, Vohr, & Lester, 2010). Children who received PCIT showed fewer attention problems, aggressive behaviors, and externalizing and internalizing problems, as well as more child compliance and more positive parent–child interactions relative to waitlist controls. PCIT-treated parents also showed more positive parenting practices, and child and parent gains were maintained across a 4-month follow-up period.

PCIT for Infants

Drawing on the research noted earlier suggesting that PCIT, without modification, can be effective for children with comorbid oppositional defiant disorder (ODD) and intellectual disability (Bagner & Eyberg, 2007), as well as for young children (ages 18–60 months) born prematurely (Bagner et al., 2010), more recent research conducted by Bagner and colleagues has extended PCIT approaches to even younger children. In one open-pilot trial, Bagner, Rodríguez, Blake, and Rosa-Olivares (2013) demonstrated promising results for a home-based PCIT adaptation for at-risk infants (12–15 months old), using only the CDI module, with minor adaptations for developmental compatibility with this younger developmental level. For example, given the reduced receptive language abilities in infants, parents were encouraged to use nonverbal praise (e.g., clapping) to accompany their verbal praise, and to repeat/

reflect positive infant vocalizations and not just words. As this was a home-based intervention, therapists spoke to the parent discreetly from nearby rather than using the bug-in-the-ear technique, as supported in pilot research (Ware, McNeil, Masse, & Stevens, 2008).

Initial results from this open-pilot trial were promising—almost 90% of families completed the program, and completers reported high treatment satisfaction and improved parent–child relationships; most parents reported considerable improvements in infant behavior problems as well. In addition, Bagner and colleagues (2015) recently completed an RCT (n = 60) examining this program relative to standard pediatric primary care. Results showed that their PCIT adaptation for infants resulted in significantly greater improvements in both externalizing and internalizing symptoms, as well greater child compliance and more positive parenting, relative to youth who simply received standard pediatric primary care.

AREAS FOR FURTHER STUDY

Next, we turn our attention to emerging PCIT-related protocols that are in the early stages of development or evaluation: (1) Internet-delivered PCIT; (2) teacher–child interaction training; and (3) PCIT for selective mutism. We conclude with a brief discussion and suggestions for future directions to expand this work.

Internet-Delivered PCIT

One of the more exciting adaptations of PCIT in recent years has been the advent of Internet-delivered PCIT (I-PCIT; Comer et al., 2015), which extends the reach of PCIT to families in need, regardless of their geographic proximity to a PCIT provider (Elkins & Comer, 2014). Despite the development and rigorous evaluation of PCIT, sizable gaps persist between services in experimental settings and those available in community practice settings (Comer & Barlow, 2014). As a consequence of geographic disparities in expert care availability, after onset of ODD, the median delay in treatment initiation is 4 years among individuals receiving care (Wang et al., 2005), and only 6% of affected individuals make initial treatment contact in the first 5 years. Only one-third of individuals with ODD will *ever* receive mental health care (Wang et al., 2005), and among preschoolers with any DBD, only 20% *ever* actually receive treatment (Pavuluri, Luk, & McGee, 1996). Those who do receive care do not necessarily receive evidence-based treatments such as PCIT.

To address these concerns, recent years have seen a dramatic increase in behavioral telehealth programs leveraging new technologies to overcome traditional geographic barriers to expert care (Comer, 2015; Comer & Barlow, 2014; Comer, Elkins, Chan, & Jones, 2014; Comer & Myers, 2016; Crum & Comer, 2015; Myers & Comer, in press). It has been suggested that PCIT

is particularly amenable to a Web format given that, by design, the therapist conducts live observation and feedback from another room via a parent-worn bug-in-the-ear device (Comer et al., 2015); that is, even in standard clinic-based PCIT, the therapist is predominantly separated from the family in order to foster naturalistic family interactions, so relative to other clinic-based treatments, the transition to a Web-based format may be more straightforward than formats for other clinic-based protocols.

Using videoconferencing, webcams, and wireless Bluetooth earpieces, I-PCIT therapists can remotely provide in-the-moment feedback to parents directly in their home during real-time parent–child interactions, regardless of a family's proximity to an expert clinic. Moreover, treating families in their own homes may even enhance the ecological validity of treatment by affording live observation and feedback in the very settings in which child behaviors are problematic. Comer and colleagues (2015) present a logistical overview of I-PCIT with video illustrations, and consider key matters related to I-PCIT equipment, videoconferencing software, room set-up and lighting, and therapeutic process and rapport. In addition, more general telehealth considerations related to hardware, security, risk management, ethics, training, and billing can be found elsewhere (Chou, Comer, Turvey, Karr, & Spargo, 2015; Comer & Barlow, 2014; Kramer, Kinn, & Mishkind, 2015). A recent RCT comparing I-PCIT to standard clinic-based PCIT (n = 40) is currently in its final stages.

Teacher–Child Interaction Training

Children with behavior problems at home are likely to exhibit similar problems in academic settings (e.g., Winsler & Wallace, 2002), and meta-analytic evidence demonstrates that preventive classroom interventions are helpful in mediating the risk for the development of behavioral problems in youth (Wilson, Gottfredson, & Najaka, 2001). Moreover, given that most children in need of psychological treatment do not receive adequate outpatient care (Owens et al., 2002; Stephenson, 2000), school-based interventions may offer a promising avenue to reach underserved youth (i.e., Atkins et al., 2006; Ginsburg & Drake, 2002).

In response to this need, a school-based adaptation of PCIT, teacher–child interaction training (TCIT) was developed as a universal prevention program to address behavioral problems in preschool classrooms (Gershenson, Lyon, & Budd, 2010; Lyon et al., 2009). Through targeting the teacher–child relationship, TCIT aims to improve the functioning of children in the preschool classroom by providing teachers with skills to increase warmth, enhance communication, and improve behavior management. TCIT retains several of the features of traditional PCIT, including the two-stage intervention format, the CDI phase and use of the PRIDE skills, "homework" assignments, and live skills coaching, but it incorporates key protocol adaptations tailored to the classroom setting. For example, teachers often receive didactic training in

TCIT through a group format rather than through individual Teach sessions, and TCIT trainers provide live coaching and feedback in the classroom as they "shadow" teachers throughout their day, rather than coaching from behind a one-way mirror. Additionally, the PDI component of the intervention is termed TDI (teacher-directed interaction), which differs substantially from PDI. TDI emphasizes the use of differential social attention and clear, direct commands to address child misbehavior, and the TCIT discipline strategy is termed "Sit and Watch" rather than time-out. The Sit and Watch procedure typically involves placing children in a brief time-out on the periphery of the classroom activity as a consequence of misbehavior, and the specifics of the procedure are determined collaboratively by teachers and trainers to maximize the chance of successful implementation within each teacher's classroom. For example, teachers and trainers collaboratively determine the specific problem behaviors they hope to target in TDI, the length of time a child should spend in Sit and Watch, and appropriate consequences for refusing to remain in Sit and Watch.

Early adaptations of TCIT evaluated via case studies targeting individual children (McIntosh, Rizza, & Bliss, 2000) and single classrooms (Filcheck, McNeil, Greco, & Bernard, 2004) provide preliminary support for this adaptation. More recent work has expanded the reach of TCIT to multiple classrooms and multiple teachers. Results of a two-stage multiple-baseline study indicate that TCIT was effective in increasing preschool teachers' use of positive attention strategies and consistent discipline strategies, and that this method was viewed as acceptable by teachers (Lyon et al., 2009). Similarly, results of a pilot study involving kindergarten and first-grade teachers found that TCIT was associated with similar increases in teachers' use of positive attention, as well as decreases in negative attention and distress associated with disruptive child behavior (Fernandez et al., 2015).

PCIT for Selective Mutism

Building on the promise of PCIT-related approaches to address early childhood anxiety disorders described earlier, researchers have extended elements of PCIT to target children with selective mutism (SM). SM is an anxiety disorder in which children consistently do not speak in certain social situations, despite speaking in other settings. The PCIT approach is well suited to address the needs of children with SM for several reasons. First, the onset of the disorder typically occurs prior to age 3, with children accessing treatment most often between ages 5 and 7 (Keeton, 2013); thus, the PCIT model is developmentally appropriate for this cohort (see Carpenter et al., 2014). Second, because children with SM typically speak with their parents but not with others, a behavioral parent training approach is helpful for this population given that the parent is the necessary agent of change in encouraging speaking behavior. Third, because children with SM likely will not speak to clinicians, forms of therapy that require verbal interactions to participate in treatment are likely less helpful than a behavioral parent training model.

PCIT for SM utilizes both individual and group therapy formats to

increase child verbal behavior. As with traditional PCIT, individual treatment begins with CDI coached via bug-in-the-ear technology. Given that the therapist's presence in the room often provokes child silence, this PCIT model allows the therapist to teach parents treatment skills from outside of the room and also to observe the child's naturalistic verbal behavior with parents. During CDI for SM, parents are coached to model appropriate verbal behavior, provide praise and attention for verbalizations, and to minimize negative reinforcement of nonverbal behavior. They are also instructed to avoid questions, criticism, and "mind reading" (i.e., "You seem like you want the marker"), while providing enthusiastic labeled praise and reflection of each verbalization.

In place of PDI, PCIT for SM involves verbal-directed interaction (VDI), during which parents are taught how to deliver effective prompts to speak in a manner that is more likely to elicit a verbal response (Kurtz, Comer, Gallagher, Hudson, & Kendall, 2013). Specifically, as open-ended questions (e.g., "What would you like to eat?") and forced-choice questions (e.g., "Would you like the apple or the yogurt?") are more likely to lead to a verbal response than a yes–no question (which can be answered nonverbally; Kurtz, Comer, & Masty, 2007), parents are taught to distinguish between these types of questions (Kurtz et al., 2013; see also Carpenter et al., 2014). They are then instructed to proceed sequentially through different types of questions to maximize the chance that the child will answer, and to avoid negatively reinforcing silence. In this model, the therapist gradually fades into the treatment, using the same CDI and VDI techniques to encourage and reward speaking behavior.

This population often benefits from participating in group therapy as an adjunct to individual parent–child treatment. Recent years have seen a rise in the use of intensive treatment camp-based formats, during which children with SM participate in several consecutive full days of treatment with same-age peers (Furr et al., 2012; Kurtz, 2012). Clinician-counselors shape verbal behavior using CDI and VDI techniques throughout the day as the group engages in developmentally appropriate activities to promote speaking and social engagement. This approach allows children with SM to practice speaking with same-age peers in a setting that more closely resembles school or camp, serving both as an exposure to anxiety-provoking situations from their daily life, and as an opportunity for peer support and modeling. Although controlled trials are needed, preliminary evaluations of such PCIT adaptations for SM provide important initial support, with increases in child verbalizations between pre- and posttreatment time points demonstrated through both single-case and open-trial designs (e.g., Furr et al., 2012; Mele & Kurtz, 2013).

CONCLUSIONS

Recent estimates indicate that 1 in 5 preschoolers meet criteria for a psychological disorder (Carter, Wagmiller, Gray, McCarthy, & Briggs-Gowan,

2010). Early evidence-based intervention is crucial, particularly given concerning trends toward increased use of unsupported treatment regimens to manage young children with mental health concerns (e.g., Comer, Olfson, & Mojtabai, 2010; Zito et al., 2007). Given the preponderance of data supporting the role of PCIT in the effective management of early child behavior problems, and the growing body of evidence supporting the promise of PCIT-related adaptations and modifications for the treatment of a range of early childhood mental health problems, this family of psychosocial interventions may be poised to offer a meaningful public health impact to ameliorate the suffering of young children coping with a variety of mental health concerns across diverse settings.

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12

Cognitive-Behavioral Therapies

Devi Miron
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Internalizing disorders such as anxiety disorders, obsessive–compulsive disorder (OCD), and posttraumatic stress disorder (PTSD) in children who are 6 years of age and younger historically have been viewed as transient adjustment difficulties (for reviews, see Cohen & Mannarino, 1996a; Scheeringa, 2009; Hirshfeld-Becker, Micco, Mazursky, Bruett, & Henin, 2011). Mounting evidence suggests, however, that these problems in young children may be as common, impairing, and persistent as those in older children, indicating the need to intervene early (Scheeringa, Zeanah, Myers, & Putnam, 2005; Egger & Angold, 2006; Hirshfeld-Becker et al., 2011).

There has been growing interest in extending cognitive-behavioral therapy (CBT) approaches to younger children. In this chapter, we consider the developmental issues involved in utilizing CBT with very young children, specifically, ages 3 to 6 years. Throughout the chapter, we use the preschool PTSD treatment (PPT) manual, a CBT manual developed by Scheeringa, Amaya-Jackson, and Cohen (2002) to treat PTSD in 3- through 6-year-old children, to illustrate how these issues can be addressed with CBT. In addition, we review the extant literature on CBT protocols for addressing anxiety disorders, OCD, and exposure to trauma in this age group. A review of the treatment of depression in young children is not included; although there is substantial evidence to suggest that young children can suffer from depression, there have been no randomized controlled trials on the use of CBT to treat young children with depression.

DEVELOPMENTAL CONSIDERATIONS FOR USING CBT WITH YOUNG CHILDREN

A commonly expressed belief is that young children are not developmentally capable of participating in CBT (Schum, 2006; Grave & Blissett, 2004). This belief is based on Piagetian developmental theory, which posited that children, roughly between the ages of 2 and 7 years, are in a prelogical stage of cognitive development. However, some suggest that Piaget underestimated preoperational children's skills. Furthermore, post-Piagetian theorists have moved away from a rigid stage model.

In their case reports of a 49-month-old boy and a 57-month-old boy treated with CBT for PTSD, Scheeringa et al. (2007) concluded, "Even though young children are still developing the capacities to self-reflect and cooperate in treatment, they can engage in structured therapy, cooperate with exposure exercises, and voluntarily use relaxation exercises for a targeted end" (p. 635). Also, randomized controlled trials have demonstrated the effectiveness of CBT in treating trauma-related problems in young children (Cohen & Mannarino, 1996a; Deblinger, Stauffer, & Steer, 2001; Scheeringa, Weems, Cohen, Amaya-Jackson, & Guthrie, 2011). Thus, it seems that there are many components of CBT in which young children can engage.

Abstract Understanding of Disorders

In using direct (vs. indirect) therapies such as CBT, it is helpful if children have a metacognitive understanding of their problems and the need to change them. Most CBT protocols involve frank discussions of disorders, impaired thinking, and maladaptive behavior with clients, in order for the therapists and clients to collaborate on treatment plans. Children who are 6 years and under may not be good reporters of their anxiety symptoms, and they have an undeveloped sense of time that might prohibit them from reporting on their duration or frequency of symptoms or impairments in functioning (Hirshfeld-Becker et al., 2011).

In a case study of a child with OCD, Labouliere, Arnold, Storch, and Lewin (2014) described a 4-year-old boy as being similar to many young children with OCD in having "no insight" into his difficulties. They concluded that traditional individual CBT was not appropriate for the child due to his cognitive capacity and level of insight. Yet the boy was able to express that he wanted his family to "make the bad feelings go away" and improve his family and peer relationships. Thus, the authors incorporated evidence-based elements of individual CBT, including psychoeducation, establishment of treatment goals, exposure and response prevention, developmentally appropriate cognitive restructuring, and between-session homework in a successful family-focused intervention.

In the PPT manual, therapists are instructed to employ pictorial representations of symptoms of PTSD during psychoeducation of PTSD. These

pictorial aids depict children in various situations who are experiencing PTSD symptoms such as intrusive recollections of traumatic events (e.g., car accidents, physical abuse, and witnessing domestic violence). Rather than use the pictorial aids to elicit symptoms, Scheeringa and colleagues (2011) demonstrated the feasibility of using this technique to teach young children about their symptoms.

Ability for Self-Reflection and Understanding Metaphors

One requirement for participating in CBT is self-reflection. Certainly, parents can report on whether their children's observable behaviors are improving, but in order to effectively participate in CBT, young children need to be able to self-identify feelings and, to some extent, be able to reflect on the cause of those feelings. A typical 5-year-old can understand the difference between mental and physical states and has a causal–explanatory framework for the interaction between mental states and behavior. However, a child with less-developed metacognitive function is likely to be less successful at these operations, both in a therapeutic context and in everyday functioning. In lieu of well-developed metacognition and introspection skills, younger children tend to prefer active strategies to identify and manage emotions, as well as to gain new coping skills.

One strategy that may assist young children in self-reflection about their thoughts, feelings, and behaviors is to employ analogy and metaphor to help them cognitively externalize symptoms from themselves. For example, in the 'ACTION' protocol for treating depression in middle childhood, Stark and colleagues (2007) used the metaphor of the "Muck Monster" when talking about depression; therapists teach clients to "not get stuck in the muck" with negative thinking. March and Mulle (1998) taught older children to "run OCD off my land." In their adaptation of the Fun FRIENDS program for treating and preventing anxiety disorders, Pahl and Barrett (2007), using a similar strategy, trained 4- to 6-year-olds to distinguish "red thoughts" (negative cognitions) and "green thoughts" (positive cognitions), and to generate "green thoughts," reinforced by the use of puppets. Through the use of metaphor, children can be taught to judge the extent to which symptoms are present or whether they are "stuck."

Capacity to Self-Rate Gradations of Anxiety and Other Emotions and the Use of Coping Strategies

Hirshfeld-Becker and colleagues (2011) advised that because young children are *unable* [our emphasis] to understand subjective units of distress (SUDS) ratings or to understand the fear thermometers that are useful with older children, it can be useful to introduce simpler pictorial means of rating anxiety. Most children this age are able to understand the concept of size and are able to identify "small, medium, and large" feelings. Scheeringa and colleagues

(2011) effectively used a 3-point rating scale rather than the often-used 10-point scale with 3- to 6-year-old children in their CBT for PTSD treatment.

The skill of rating internal distress is important during the exposure exercises that are central to CBT for PTSD and anxiety problems. Exposure exercises are meant to produce modest levels of distress, so that children can use their new coping and relaxation skills to decrease their levels of distress. Children learn to notice when distress increases due to triggers and when distress decreases due to the implementation of successful coping strategies. While these skills are important for CBT, they are also likely to be important for long-term stability of treatment gains, because children will have learned to recognize early distress better, and they will be more likely to employ their new coping strategies in the future, before negative feelings become unmanageable.

Addressing Maladaptive Cognitions with Positive Self-Talk

"Automatic negative thoughts" are overgeneralized negative thoughts about one's self, others, or the world. It is a common technique in CBT to teach clients to recognize these thoughts, then develop more realistic replacement thoughts. In a study of children with average IQ, 5- to 7-year-olds generated alternative explanations for why an ambiguous social event occurred, named and recognized emotions, and connected thoughts and feelings using cartoons with thought bubbles (Doherr, Reynolds, Wetherly, & Evans, 2005). Hirshfeld-Becker et al. (2008), using puppets to facilitate discussions, showed that anxious 4- to 7-year-olds were able to choose between thoughts that made them feel more or less brave in hypothetical situations. McMurray, Lucas, Arbes-Duprey, and Wright (1985) taught children as young as 3 years old, with no prior dental treatment, to learn to apply new coping skills for relaxation effectively, including deep breathing, cue words "calm" and "nice," positive imagery, and to say to themselves, "I will be all right in just a little while. Everything is going to be all right," prior to having a cavity filled.

Besides the specific task of identifying maladaptive cognitions, there are many other facets of CBT that are contingent on a certain developmental level of cognitive skills. These facets include skills for causal reasoning, perspective taking, self-reflection, verbal expression, and autobiographical memory (Scheeringa et al., 2011). For example, in Session 1 of PPT, children's PTSD symptoms are given a name and story form, which involves the cognitive tasks of self-reflection, autobiographical memory, and causal reasoning. In Session 3, children's fears are placed in a bigger context of other feelings and other situations, which also involves the cognitive tasks of self-reflection, autobiographical memory, and causal reasoning. In Sessions 6 through 10, children complete exposure exercises that require similar skills. The protocol does not require children explicitly to identify automatic negative thoughts, as do CBT protocols for depression in older individuals, but the authors advise that these thoughts are implicitly and sometimes explicitly addressed during the children's narratives of the traumatic experience.

Relaxation Training and Positive Imagery

The PPT manual (Scheeringa et al., 2002, 2011) incorporates the anxiety management skills of controlled breathing, muscle relaxation, and positive imagery. For controlled breathing, young children are taught to breathe in deeply, then exhale slowly and completely. For muscle relaxation, children are taught to make their muscles go "tight, tight," then "go loose like noodles." For positive imagery, which may be the most difficult for young children to grasp, children are instructed to think about a happy or calm place, such as a fun event, the beach, or their mother's lap. The children are then instructed to draw a picture of the happy place, then close their eyes and think about it for 15–30 seconds. The authors demonstrated that the young children were able to practice these techniques 92% of the time in the first session in which they were introduced. The percentage rose to 100% as the children gained practice in subsequent sessions (M. S. Scheeringa, personal communication, August 31, 2015).

Exposure Exercises

Several studies have demonstrated the efficacy of exposure-based approaches for addressing fears in cases of OCD, PTSD, or anxiety disorders in young children. Hirshfeld-Becker and colleagues (2008) used a number of exposure approaches to help children, ages 4 to 7 years, with social and separation anxiety in their pilot study and later in their randomized controlled trial (Hirshfeld-Becker et al., 2010). Their techniques included treasure-hunting games to practice separating from parents, glow-in-the-dark toys to practice sleeping separately from parents in a dark room, "survey" games (asking questions, noting eye color) to practice social interaction, and humorous use of role play of mistakes or rule-breaking behaviors for children with perfectionistic worries.

The most extensive use of exposure exercises with young children has been in the treatment of trauma-related problems in two randomized controlled trials (Cohen & Mannarino, 1996a; Scheeringa et al., 2011). Scheeringa and colleagues documented the feasibility of specific techniques in their study with 3- to 6-year-old children. For exposure exercises conducted in the office with drawings and narration, out of 140 therapy sessions conducted with 36 children, the children were able to cooperate with the exposure 90% of the time. For exposure exercises conducted in the office with eyes closed and children asked to imagine their traumatic experiences, children were able to cooperate 75% of the time. For exposure exercises conducted in the environment with their parents as homework assignments, the children were able to complete the exposure 82% of the time. Furthermore, it appeared that the 3- and 4-year-old children were just as capable of cooperating as the 5- and 6-year-old children, despite the developmental differences across that age span.

Autobiographical Memory and Narratives

Studies of normal development (e.g., Fivush & Hamond, 1990) and studies of help-seeking clinical samples (e.g., Terr, 1988) converge on the timeline that the capacity to develop narratives of autobiographical events do not emerge until approximately 36 months of age. This likely explains why there are no known published cases of PTSD in persons younger than 3 years of age. Some suggest that using techniques to elicit narratives from children between ages 5 and 8 years can improve their cognitive capacity to benefit from creatively delivered forms of CBT, because these narratives represent inner reflections of their thoughts and feelings (Grave & Blissett, 2004). Furthermore, Scheeringa and colleagues (2011) demonstrated that 67% of 3-year-old children with PTSD could generate at least three details of their traumatic events when asked to do so the first time; 82% of 4-year-olds, 80% of 5-year-olds, and 100% of 6-year-olds could perform this task when asked the first time. These percentages for the younger children increased with practice during exposure exercises in subsequent sessions (M. S. Scheeringa, personal communication, August 31, 2015).

Another way to assist young children with recall of past memories and construction of new interpretations of past experiences is through drawing. Drawing is a common technique to assist younger children with recall of past memories, to help express internalized thoughts and feelings (Gross & Hayne, 1998), and in particular to facilitate the expression of painful traumatic memories (Malchiodi, 1997; Steele, 2002). Scheeringa and colleagues (2011) used drawing to aid children, ages 3 to 6 years, in recounting traumatic experiences. Here, drawing was also used to assist with completing imaginal exposure exercises to practice skills for coping with PTSD symptoms.

Managing Cooperation

A significant challenge in working with young children, especially those with emotional and behavioral difficulties, can be eliciting cooperation. For example, in their case study report of a 4-year-old boy with OCD, Labouliere and colleagues (2014) noted that "complicating factors" of the child's treatment included the child's "oppositional, defiant, and aggressive behavior." To address the behaviors, this child's treatment incorporated 20–30 minutes of child-directed play with his parents, as well as behavioral management techniques, such as planned ignoring of his engagement in compulsions or other negative behaviors and differential reinforcement of more appropriate behaviors. Additionally, in their treatment of young children with anxiety, Hirshfeld-Becker and colleagues (2008) employed a variety of reinforcement and contingency plans to motivate children to practice newly learned skills for coping with social and separation anxiety.

In the PPT manual, Scheeringa and colleagues (2002, 2011) addressed how to encourage cooperation and manage behavior at home and within

sessions in a variety of ways. First, as oppositional defiant behavior is often observed in young children following a traumatic event, the manual included an optional session for targeting oppositional behaviors. This session included psychoeducation for parents about the relationship between oppositional behaviors and PTSD, as well as a discussion on possible parent tendencies to be "lenient" about discipline following their child's experience of a trauma. In addition, throughout the manual, therapists are encouraged to give the rationale for certain exercises to their young clients before asking them to follow a directive. The manual also included helpful strategies for engaging oppositional children, such as acting like an activity is fun, so that the child will want to do it.

Involvement of Parents

Involving parents in treatment with their young children is essential given the nature of parent–child relationships during the preschool years. In addition, parents can more accurately report on their child's progress in treatment. In their work with young children with anxiety disorders, Hirshfeld-Becker and colleagues (2002, 2011) made the case for including parents in treatment, especially when the parents themselves struggle with anxiety. They suggested, however, that anxious parents might not be able to assist their children effectively in managing anxiety. Reasons for involving parents in interventions for anxiety disorders in young children include the following: (1) Early intervention is an opportunity to teach parenting skills that may carry over into later childhood; (2) intervention with parents might shape more positive parental representations of their children, assuming that some anxious parents may regard their anxious children as vulnerable or fragile; and (3) parents who are involved in their children's treatment may become "keepers of knowledge," who are able to coach their children in coping with future anxiety.

Researchers also agree that parents ought to be involved in their young children's recoveries from trauma-related problems. Cohen and Mannarino (1996a) concluded that including the nonoffending parent in their individual-therapy protocol, CBT for sexually abused preschoolers, appeared "very effective" in reducing child symptoms. They reported a strong positive correlation between both parent depression and parent emotional distress scores, and child outcome posttreatment measures, independent of the type of treatment provided (Cohen & Mannarino, 1996b).

Deblinger et al. (2001) involved nonoffending parents in group therapy to learn to manage their children's symptoms following sexual abuse. The researchers found that mothers who participated in cognitive-behavioral, as compared to supportive, groups had reduced intrusive thoughts and negative emotional responses to their child's abuse.

Weems and Scheeringa (2012) found that at baseline, maternal depression was associated with higher initial child PTSD symptoms, and mothers' depression scores were reduced following treatment of their children's PTSD.

Furthermore, higher maternal depression was associated with increasing PTSD symptom trends at follow-up, suggesting potential child PTSD symptom relapse.

Researchers agree generally that parents should receive psychoeducation about their children's disorder and learn ways to identify symptoms accurately. While unproven, some researchers have even gone so far as to speculate that this new knowledge may help to prevent inadvertent accommodation or reinforcement of their children's symptoms (Hirshfeld-Becker & Beiderman, 2002; Freeman, Sapyta, Garcia, Compton, Khanna, et al., 2014; Lewin et al., 2014). Hirshfeld-Becker and Beiderman (2002) also suggested that parents can be taught to become their children's therapists by learning principles of graduated exposure and planning exposures for their children's current and future anxiety triggers. By engaging in this process, parents can learn to reward small steps toward success and also may become desensitized to their children's anxiety and come to view their children as more resilient.

In their treatment protocol for young children with PTSD, Scheeringa and colleagues (2002, 2011) operationalize parent involvement systematically and session by session. The protocol also built in discussions of motivation and treatment compliance with parents in nearly every session. The parent's reluctance to participate in therapy is validated, systematically rated on a weekly basis, and addressed in more depth when needed.

EVIDENCE FROM STUDIES OF CBT TREATMENT WITH YOUNG CHILDREN

Anxiety Disorders

A substantial amount of research on CBT for young children has focused on anxiety disorders, including specific phobias, social phobia, generalized anxiety disorder (GAD), and separation anxiety disorder. To our knowledge, only two trials have involved providing CBT directly to young children with anxiety disorders (Waters, Ford, Wharton, & Cobham, 2009; Hirshfeld-Becker et al., 2010) and are described below.

Waters and colleagues (2009) compared a parent CBT group only to a parent CBT group plus child CBT group using the Take ACTION program, a CBT program for children ages 4–18 years with anxiety disorders (Waters, Donaldson, & Zimmer-Gembeck, 2008; Waters, Wharton, Zimmer-Gembeck, & Craske, 2008). Both intervention groups were also compared to a waitlist control condition. The trial involved children, ages 4–8 years, who had been diagnosed with specific phobia, social phobia, GAD, or separation anxiety disorder, using a structured interview.

Parents in the parent-only condition received 10 weekly CBT sessions in a group format. Children and parents in the parent + child condition each received 10 weekly CBT group sessions: The treatment for children included psychoeducation about anxiety and bodily reactions associated with being

anxious; relaxation training; identifying anxious self-talk and assisting children to use coping statements; graded exposure; the development of problem-solving skills; the identification of children's support networks; and social skills training to develop confident nonverbal behavior, assertiveness, and strategies for dealing with bullies. Both the parent-only and parent + child conditions involved the same homework assignments. Session content for the parent group was identical in both active conditions. Booster sessions were held for both groups 8 weeks postintervention.

Completer analyses were conducted using data from 23 children in the parent + child condition and 25 in the parent-only condition, and were compared to 11 children in the waitlist condition. Seventy-four percent of children in the parent + child condition, 84% in the parent-only condition, and 18% of the wait-list children no longer met criteria for their principal anxiety diagnosis posttreatment. The differences between each active treatment group as compared with the wait-list condition were significant. The two active conditions did not differ significantly. At 6-month follow-up, 89% of children in the parent + child and 100% of children in the parent-only condition no longer met criteria for their principal anxiety disorder diagnosis based on completer analyses. While these findings are promising, data were not reported separately for children under age 6 years, so it is difficult to draw conclusions about the effectiveness of the treatment for younger children.

Hirshfeld-Becker and colleagues (2010) used individual parent-only coupled with child–parent sessions in their intervention designed to address anxiety. Sixty-four children, ages 4–7 years, with an anxiety disorder were randomized to either treatment condition. The manualized intervention, *Being Brave: A Program for Coping with Anxiety for Young Children and Their Parents* (Hirshfeld-Becker & Beiderman, 2002; Hirshfeld-Becker et al., 2008, 2010) was adapted from the Coping Cat program (Kendall, Kane, Howard, & Siqueland, 1992), which involved relaxation training, cognitive restructuring, and *in vivo* exposure. The researchers adapted the protocol for young children in several ways, including the use of age-appropriate self-instructive strategies to manage anxiety and exposure exercises modified to include games and immediate positive reinforcement; greater parental involvement in reinforcing coping techniques; inclusion of parental anxiety management strategies; and inclusion of parent skills training. The model was developed based on the principle that graded exposure is the primary means of reducing anxiety symptoms in children, and that young children need to understand the rationale for treatment, which was presented through age-appropriate stories. Children were also taught to rehearse basic coping strategies to facilitate exposure and were motivated to practice exposure exercises through a contingent reinforcement plan. Six parent-only sessions were completed prior to the initiation of parent–child sessions and covered psychoeducation about anxiety management strategies, parenting an anxious child, and planning and completing exposure exercises. The number of parent–child sessions was as flexible as needed to complete exposure exercises to a number of feared situations, with a minimum of eight sessions and a maximum of 13.

Fifty-seven of the 64 children enrolled in the study completed the intervention. The proportion of children completing each condition who were rated by the clinician evaluator as *much improved* or *very much improved* was 69% (20/29) for the CBT children and 32% (9/28) for the controls. Among completers, 59% of the CBT group and 18% of control group children were rated as free of anxiety disorders. At 1-year follow-up, 24/29 (83%) of the CBT treatment completers were rated as *very much improved* or *much improved* from their baseline presentation, and none was rated as unchanged or worse.

Future studies need to assess the extent to which early intervention with CBT can mitigate the course of anxiety disorders or the onset of new anxiety disorders later in childhood and in adolescence. Furthermore, it is not clear whether the small proportion of nonresponders in these studies would benefit from a higher-intensity or different format of CBT. Finally, the findings for those participants under age 6 years were not reported separately, which makes it difficult to draw conclusions for this age group.

Obsessive–Compulsive Disorder

A number of case studies and case series (Ginsburg, Burstein, Becker, & Drake, 2011; Comer et al., 2014; Labouliere et al., 2014) have been published involving CBT with young children diagnosed with OCD. There has been one randomized controlled trial (Freeman et al., 2014) and one randomized controlled pilot study (Lewin et al., 2014), both of which provided CBT directly to young children and their caregivers (as opposed to providing therapy to the parent only).

Both of the randomized studies involved parents heavily because of logistical issues of parental support needed for conducting exposure plus response prevention (E/RP) exercises in the home, and the investigators' beliefs that parental accommodation of OCD behaviors played a facilitating role. In the Pediatric Obsessive Compulsive Treatment Study for Young Children (POTS Jr), Freeman and colleagues (2008, 2014) examined the relative efficacy of family-based CBT (FB-CBT) involving E/RP versus another active treatment control condition, family-based relaxation treatment (FB-RT). The POTS Jr study was conducted at three academic medical centers between 2006 and 2011, and involved 127 pediatric outpatients, ages 5–8 years who had a primary diagnosis of OCD and a Children's Yale–Brown Obsessive Compulsive Scale (CYBOCS) total score of 16 or higher. Fifty-four (42.5%) participants were 5 or 6 years old.

The participants were randomly assigned to FB-CBT or FB-RT. Both treatments involved 12 sessions over 14 weeks. The first two sessions were conducted with parents only, and the rest were held with both children and parents jointly. The primary components of FB-CBT included (1) psychoeducation about OCD's neurobiology, correction of misattributions, identifying OCD behaviors, and rationale for treatment; (2) behavior management skills training for parents, including behavioral management of the children's OCD symptoms with differential attention, modeling, and scaffolding of the

children's use of tools towards self-regulation; (3) teaching the children to externalize OCD; (4) E/RP; and (5) family process components. Parents were actively involved during in-session and home-based E/RP.

Key modifications to fit the age group included (1) involving parents in all phases of treatment; (2) tailoring psychoeducation, exposures, and homework to meet the children's unique developmental level; and (3) focusing on the family context such as the parents' responses to their children's anxieties (Freeman et al., 2012).

FB-RT involved (1) psychoeducation about the relationship between stress management and anxiety, and the rationale for treatment; (2) the implementation of a reward system; (3) education for children to identify feelings, with an emphasis on anxiety; and (4) relaxation training comprising progressive muscle relaxation and guided imagery.

The results indicated that FB-CBT was superior to FB-RT on both the CYBOCS and the Clinical Global Impression—Improvement (CGI-I) scale. Seventy-two percent of the participants for the FB-CBT group and 41% for the FB-RT group were rated as *very much improved* or *much improved* on the CGI-I scale immediately posttreatment. In addition, the effect size difference between FB-CBT and FB-RT on the Compulsive Disorder Impact Scale—Revised scale was medium, 0.42 (95% confidence interval [CI], 0.06–0.77) and on the CYBOCS was large, 0.84 (95% CI, 0.62–1.06).

Of note, the results of the study were similar or superior to studies involving older age groups (Barrett, Healy-Farrell, & March, 2004; Piacentini et al., 2011), suggesting that young children can indeed benefit from CBT aimed at reducing OCD symptoms and impairment. The authors concluded that the young children involved in their study had "real" and impairing OCD warranting more than a "watch and wait" approach (Freeman et al., 2014, p. 696). However, although the authors reported the number of children ages 5 and 6 years, they did not report results separately for this group.

In their randomized controlled pilot trial, Lewin and colleagues (2014) extended the study of family-based E/RP therapy downward for young children with OCD below age 5 years. Thirty-one children, ages 3–8 years, with a primary diagnosis of OCD were randomized to E/RP (n = 17) or treatment as usual (TAU; n = 14). Eleven (35%) of the children were below age 5 years (the "younger" group), and some analyses were reported separately for this group. Participants in the E/RP condition received 12 sessions of family-based E/RP twice weekly over 6 weeks.

The intervention targeted OCD symptoms, as well as accommodation by family members. All sessions were conducted with the children and at least one primary caregiver present at all times. Treatment components included psychoeducation for parents and children (allying against OCD; introducing developmentally appropriate metaphors/examples), parent tools (e.g., development of a rewards program, differential reinforcement, extinction, and modeling), E/RP, and relapse prevention planning based on previous work (Freeman et al., 2008). Additionally, less emphasis was placed on cognitive elements

of the treatment and more focus was placed on addressing parent behaviors, including reducing accommodation, training in extinction-based treatment, and implementing E/RP independently at home. Behavioral-based parent training principles were embedded in E/RP practice as needed. Families in the TAU group were instructed to continue their prior interventions (including therapy and pharmacological interventions) or to select a new treatment not affiliated with the study.

Perhaps somewhat surprising given the perception that E/RP is challenging to conduct with young children, there was no attrition in the E/RP group, and treatment satisfaction ratings were high. The results of the between-group analyses were that children in the E/RP condition displayed a greater remission in OCD symptoms compared with the TAU group on all outcome measures. For example, 58.8% of youth in the E/RP group showed symptom remission on the CYBOCS compared with 0% in the TAU group. In addition, categorical treatment response rates (based on the CGI-I) were higher for the E/RP group (64.7%, $n = 11$) as compared with the TAU group (7.1%, $n = 1$). All participants retained responder status at 1-month follow- up, and 88.9% retained treatment responder status at 3-month follow-up. There was a higher percentage of treatment responders in the older group (age 5 years and older; 78.6%) versus those in the younger group (50%). Based on the CGI–Severity scale, 33% of younger children were remitters, compared to 36.3% of the older group.

The findings from this trial further supported the acceptability, feasibility, and efficacy of E/RP for OCD in early childhood. Although children ages 5–8 years had a higher percentage of treatment responders than did the younger group, remission rates were similar across the two ages groups. The authors concluded that the results of their study further debunked speculation that E/RP is not indicated or is even coercive for younger children. They supported the idea that the behavioral component of E/RP was the essential mechanism for change versus any sophisticated cognitive intervention, and they speculated that targeting parent accommodation is integral given the dependence of young children on their caregivers. Furthermore, the authors concluded that it is not necessary to spend several sessions providing the rationale of E/RP to the child when this can be explained by the parent.

Trauma-Related Problems

To date, three groups have demonstrated the effectiveness of CBT techniques in young traumatized children: Cohen and Mannarino (1996a) and Deblinger et al. (2001) showed superiority in treatment outcome of CBT techniques in randomized trials. Their groups were limited to sexually abused children, and children did not have to have PTSD to be included. Scheeringa and colleagues (2011) demonstrated effectiveness of CBT techniques for young children with a diagnosis of PTSD following a variety of types of traumatic events.

Cohen and Mannarino (1996a) manualized a weekly 12-session CBT

protocol for sexually abused preschool children (CBT-SAP). Sixty-seven 3- to 6-year-old children were randomized to either CBT-SAP or nondirective supportive therapy (NST). Each group completed 12 sessions of about 90 minutes' duration. The therapist spent 50 minutes with the parents, then 30–40 minutes with the child.

In addition to using traditional CBT techniques with the children, such as cognitive reframing, thought stopping, and positive imagery, the CBT-SAP sessions included time spent with the children's mothers. The CBT-SAP protocol systematically addressed the mothers' ambivalence in belief about their children's abuse, feeling that the child was "damaged," provision of appropriate emotional support to the children, management of inappropriate child behaviors (including regressive and sexual behaviors), with contingent reinforcement programs and parent training, management of fear and anxiety symptoms, issues about the mothers' own histories of abuse (if applicable), and legal issues. Specific child issues addressed in the model included safety education and assertiveness training, identification of appropriate versus inappropriate touching, attributions regarding the abuse, ambivalent feelings toward the perpetrator, regressive and inappropriate behaviors, and fear and anxiety (Cohen & Mannarino, 1996a).

The control condition involved NST. NST therapists provided support, built rapport, and encouraged the expression of feelings; however, NST was not designed specifically to address sexual abuse issues.

Thirty-nine children completed the CBT-SAP protocol and 28 completed the NST protocol. At the end of treatment, compared with the NST group, the CBT-SAP group displayed fewer sexual and other problematic behaviors, and had lower scores on two of the four broad-band scales on the Child Behavior Checklist (CBCL; Achenbach & Edelbrock, 1983). In addition, pre- to posttreatment comparisons revealed that the CBT-SAP group significantly improved on all of the outcome measures except the CBCL Social Competence scale, whereas the NST group improved on only a weekly behavior rating scale. Initial scores on the children's self-report measure of affective scores were low for both groups, and there was no significant change posttreatment for either group. However, the children in the CBT-SAP group had significantly lower sexualized behaviors than did those in the NST group (e.g., six children in the NST group were removed from the study due to inappropriate sexualized behavior, compared with none in the CBT-SAP group). Seven NST children sought additional treatment following the intervention, compared with only one child from the CBT-SAP group. The authors suggested that the CBT-SAP protocol was effective at eliminating inappropriate sexual behaviors within an acceptable number (two) of treatment sessions.

This study provided strong support that children as young as 3 years of age can understand and utilize cognitive-behavioral techniques to address issues related to sexual abuse. The authors emphasized the need to address sexual abuse directly with young children and their parents, especially when the abuse has been validated prior to beginning treatment. They also

recommended a prompt implementation of a contingency reinforcement program when sexualized behaviors are present.

Deblinger et al. (2001) compared supportive and CBT group therapies for 44 children, ages 2–8 years (mean = 5.45 years, *SD* = 1.47), who had experienced sexual abuse and their nonoffending mothers. The parents and children in both the supportive and CBT groups met for a total of 11 sessions, each 1 hour and 45 minutes in duration. In addition, the CBT group met for an additional 15 minutes each week for a joint parent–child activity. The CBT parent group was highly structured and covered education and mother's coping with their child's sexual abuse; encouraging parents to talk openly about their children's sexual abuse in the group; learning ways to talk about the abuse with their children and providing age-appropriate education about sexuality to them; and behavior management. The supportive group sessions were much less structured, and weekly topics were identified by the group members themselves. Parents in this condition were not given specific information about cognitive coping, gradual exposure, or behavior management.

The two children's groups were similar in content. Therapists assisted children with learning (1) to communicate about and cope with their feelings; (2) to identify "OK" and "not OK" touches; and (3) abuse response skills. Children were not asked specifically to talk about their sexual abuse experiences in either group. The format of the supportive group was didactic, whereas therapists in the CBT group used a more interactive behavioral-therapy format, presenting the information using an interactive workbook, role plays, behavioral rehearsal, and joint parent–child exercises.

Mothers who participated in the CBT group reported (1) a significantly greater reduction in intrusive thoughts about their children being sexually abused and (2) a significantly greater reduction in their levels of emotional distress as compared with mothers who participated in the supportive group. Furthermore, the effect sizes were greater for mothers and children who completed CBT versus supportive group therapy for eight of the 11 outcome measures. In addition, parents in the CBT group reported fewer intrusive thoughts and negative emotional reactions about their children's sexual abuse, in addition to greater satisfaction with treatment, than the parents in the supportive group.

Regarding the children's symptoms and behaviors, on the Child Sexual Behavior Inventory, the effect size was moderate (0.74) for the CBT group versus small (0.47) for the NST group. However, the children in the CBT group did not demonstrate significantly greater reductions in PTSD symptoms compared with their peers in the supportive group. Both groups demonstrated significant PTSD improvements over time despite not having been encouraged to discuss their abuse experiences directly in the group. The authors suggest that structured gradual exposure may not be a critical ingredient for therapy for very young, mildly symptomatic, sexually abused children.

One limitation of the study is that the authors did not report the number of children involved in the study who were between ages 2 and 6, or

differences in engagement in treatment or results for this age group. Given the wide range of developmental capacities within this age group, it is difficult to draw conclusions about the effectiveness of the protocol for very young sexual abuse victims.

The randomized clinical trial involving CBT for 3- to 6-year-old children with diagnosed PTSD conducted by Scheeringa and colleagues (2011) was the first to systematically collect data on the feasibility of treating young children with CBT techniques. Sixty-four children and their caregivers were randomly assigned to a 12-week CBT individual intervention or to a waitlist. The children had either experienced an acute, single blow trauma, repeated exposure to domestic violence, or had experienced Hurricane Katrina. Waitlisted children whose symptoms did not fully remit after 12 weeks were allowed to enroll in CBT. Children were reassessed at 6 months posttreatment. Children enrolled in the study were 59.5% African American and 35.1% European American, which reflects the demographics of the city in which the study took place at the time of recruitment but which is unique compared with previously published studies of early intervention CBT studies involving mostly European American children and families.

The protocol included the following components: psychoeducation about PTSD, behavior management, recognition of emotions, development of coping skills (progressive muscle relaxation, controlled breathing, and positive imagery), graduated exposures to trauma-related reminders using drawings, imaginal and *in vivo* modalities, and safety planning. The mothers of the children were present for all of Sessions 1 (psychoeducation), 2 (behavioral management), and 12 (review/graduation), and they observed the children's work with the therapists for the remaining sessions via television in a separate room, so that they could learn the material simultaneously. In addition, mothers spent the second half of Sessions 3–11 alone with the therapists. Caregivers and therapists spent this time interpreting the children's body language, and discussing and troubleshooting homework.

Using time × group analysis, the CBT group showed significant improvement in PTSD symptoms compared with the waitlist group. Time effects were significant for major depressive disorder, separation anxiety disorder, and oppositional defiant disorder, but the time × group interactions were not significant. There was no improvement for attention-deficit/hyperactivity disorder (ADHD) in either group. The effect size for PTSD was larger than those for comorbid disorders, even as effect sizes for all disorders except ADHD were moderate to large. There was an 82.4% reduction in PTSD diagnosis for the 25 treatment completers. At 6-month follow-up, the effect size increased for PTSD, while remaining fairly constant for the comorbid disorders.

Regarding feasibility of CBT techniques with young children, the 46 children who completed at least one treatment session and were rated on feasibility were judged to understand and complete 83.5% of the 1,793 possible treatment items. The authors reported that, in general, the 3-year-old children had difficulty with some tasks, such as the initial graduated exposure

sessions. Children seemed to have the most difficulty with imaginal exposures (vs. with drawing-based exposures or *in vivo* exposures). However, they completed nearly all tasks, including exposures, with time and practice. Other difficulties included rating their gradations of emotions and understanding new homework assignments, even though they were able to successfully complete homework assignments with their caregivers. In addition, using pictorial aids to educate about PTSD symptoms seemed to assist the majority of the children in understanding the concepts.

This was the first study to show effectiveness and feasibility of CBT for young children with PTSD from a variety of traumatic events. The authors noted that the attrition in this study was unusually high, possibly due, in part, to Hurricane Katrina striking the area 6 months into the study. Because of this and the relatively small sample size, the authors cautioned that any conclusions about efficacy should be considered tentative pending replication.

CONCLUSIONS

The early randomized controlled trials have indicated the effectiveness of CBT for anxiety, OCD, and PTSD, although these studies have been limited mostly to comparisons with waitlist conditions. Within these studies, and with additional evidence from carefully documented case studies, the evidence base for the feasibility and effectiveness of CBT for very young children is compelling. It is apparent that children as young as 3 years of age can participate in meaningful ways with the basic components of CBT, including the capacities to self-reflect, self-rate gradations of feelings, identify maladaptive thoughts, produce autobiographical narratives, use relaxation techniques, and engage in exposure exercises. Developmental adaptations have been used successfully with specific components and with overall methods to enhance cooperation with psychotherapy. These findings seem to outweigh considerably the doubts of those who have questioned the feasibility of CBT techniques for very young children. The techniques are inexpensive and very feasible for clinicians to learn, and they deserve widespread dissemination to benefit this population.

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13

Attachment-Based Parent–Child Relational Therapies

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> Parents don't make mistakes because they don't care, but because they care so deeply.
>
> —T. Berry Brazelton

Early attachment has long been recognized as a chief influence on social–emotional health and development during childhood and throughout the lifespan. Therefore, enhancing the quality of dyadic attachment patterns is an ideal target for evidence-based interventions with preschool-age children and their parents. In this chapter, we first provide a general discussion of attachment, followed by a summary of attachment-based assessment methods, and a description of the goals and components of most attachment-based treatments. We also describe in more detail three interventions grounded on attachment theory that have promising efficacy: the Circle of Security, child–parent psychotherapy (CPP), and Mom Power. In our discussion, we use the term "parent" to refer to biological, adoptive, or foster mothers and fathers, as well as other primary caregivers who function as a parent figure for the child. Although clinical disorders of attachment are included in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (i.e., reactive attachment disorder and disinhibited social engagement disorder; American Psychiatric Association, 2013), these diagnoses are rare and reserved for children who have experienced extremely insufficient care, and are not the focus of this chapter.

ATTACHMENT THEORY AND CLASSIFICATION

After birth, almost all aspects of an infant's development are dependent on the caregiver. Throughout infancy and toddlerhood, children make impressive strides toward independence, and by the time they begin preschool, children are described by others as having distinct personalities, and are able to identify their own, as well as others', wants and emotional states, and use an array of regulatory skills to manage their needs and conform with social norms (Denham, 2006; Marsh, Ellis, & Craven, 2002). Despite increased independence, relationships with caregivers continue to be foundational for the physical, cognitive, and social–emotional growth of preschoolers (Elicker, Englund, & Sroufe, 1992; Estrada, Arsenio, Hess, & Holloway, 1987). The characteristics of early relationships also have significant implications for long-term functioning; a supportive early caregiving environment promotes psychosocial health during adolescence and adulthood, whereas problematic early caregiving relationships increase risk for psychosocial problems, including psychiatric disorders, delinquency, and other adverse outcomes (Carlson, Jacobvitz, & Sroufe, 1995; Ingoldsby et al., 2006; Warren, Huston, Egeland, & Sroufe, 1997).

Early relationships can be understood using attachment theory (Ainsworth, Blehar, Waters, & Wall, 1978; Bowlby, 1982). "Attachment" is the innate tendency to create an enduring bond with a primary caregiver. The attachment system becomes activated during times of threat or distress, motivating the child to seek proximity or contact with the parent and signal distress, ultimately to ensure protection from danger. The parent provides protection and comfort to the child, and promotes physical safety and the child's return to well-regulated physical and psychological states. The attachment system works in concert with early exploratory, fear/wariness, and social/affiliative behavioral systems. Parental availability can enhance exploration, promote social interaction, and reduce wariness in new situations; on the other hand, activation of the attachment system (e.g., fear or distress) results in temporary inhibition of these other behavioral systems (Stafford & Zeanah, 2006).

During the first year of life infants develop an attachment relationship with their primary caregiver. Three-month-olds show differential responsiveness to their mother and by 6 months of age, children start experiencing fear of strangers. With increased locomotion, it is common to see separation distress and proximity maintenance behaviors during the second half of the first year, as well as reduced friendliness with strangers and preferential clinging to the parents when distressed (Ainsworth et al., 1978; Bowlby, 1982; Stafford & Zeanah, 2006). During the second year of life, infants form attachment relationships with other important figures (secondary caregiver, siblings, etc.). By the time children reach preschool age, they are less likely to manifest attachment needs through physical proximity or contact (Marvin & Britner, 1999). Their expanded cognitive, memory, and communication abilities help consolidate expectations about the availability and responsiveness

of the attachment figure; that is, previous child–parent interactions guide children's behavioral strategies (e.g., avoiding rather than seeking proximity) when the attachment system becomes activated. Preschoolers are also better able to understand the feelings and behavioral motivations of their caregiver, allowing a "goal-corrected partnership" in which interactions are increasingly reciprocal (Bowlby, 1982).

Initially, dyadic attachment quality is highly influenced by the parent's behavior. Sensitive, responsive, and consistent caregiving promotes a secure attachment. Children in securely attached dyads are able to signal their distress effectively and seem to expect that their needs will be met, while parents express enjoyment in the relationship and insight into the child's inner life and needs. In contrast, a pattern of maternal disengaged, dismissive, insensitive, or inconsistent behavior is often seen in dyads that are "out of sync" and classified as insecurely attached. In these dyads, the connection between the parent and child may seem weak and superficial, such that the child does not turn to the parent in times of distress or threat (e.g., an avoidant child), or dyadic interactions do not enhance regulation during times of distress (e.g., a clingy child who cannot be soothed by the parent). In more extreme situations, when caregiving is significantly disrupted, abusive, or neglectful (e.g., child maltreatment or institutional rearing), the dyad may develop a disorganized attachment, such that both parent and child do not have organized and coherent strategies that they can effectively use when the attachment system is activated. These young children face a situation in which the parent may be both the child's primary source of safety and protection and at the same time the source of threat or danger, a conflict that undermines effective coping (Main & Solomon, 1986).

A large volume of research on attachment has focused on mother–infant dyads and used the Strange Situation Procedure (SSP; Ainsworth et al., 1978) to characterize attachment quality. Ainsworth and colleagues used this separation and reunion task to evaluate the infant's affective and behavioral responses and characterize their relationship as secure (e.g., demonstrating clear proximity seeking and maintenance of contact), insecure–avoidant (e.g., little eye contact, turning body away), or insecure–ambivalent/resistant (e.g., rejecting, angry, cannot be soothed). Disorganized attachment patterns can also be assessed using the SSP. Disorganized infants appear frightened of their mother or resort to contradictory, bizarre, or self-injurious behaviors to soothe, while their mother may appear frightened, helpless, frightening, or hostile (Main & Solomon, 1986). Among normative samples, 70–85% of mother–infant dyads are securely attached, while disorganized attachment rates are as high as 81–93% among infants who are maltreated or reared in an orphanage (Cicchetti, Rogosch, & Toth, 2006).

Although developed through observations with infants, the SSP has been modified to be used with preschoolers. Cassidy, Marvin, and MacArthur Working Group (MAC; 1992) developed a classification system that closely followed the infant system advanced by Ainsworth and colleagues (1978) and

incorporated child controlling–caregiving and controlling–punitive behaviors (e.g., bossing one's mother around) as markers of disorganization. Independently, Crittenden (1983) developed the dynamic–maturational model (DMM), which first expanded the infant classification system to include a pattern of behavior that oscillates between avoidant and resistant behaviors, and was later applied to preschoolers. This system differentiates between secure, typical insecure, and atypical insecure attachment patterns. In addition, child compulsive caregiving (i.e., taking care of the caregivers' needs above one's own) and compulsive compliance are used as markers of insecure–avoidant behaviors, while controlling behaviors (threatening, disarming, aggressive, or helpless) are markers of resistant attachment.

Although fewer studies are available, rates of secure attachment in normative samples of preschoolers range from 35 to 52% (Moss, Cyr, Bureau, Tarabulsy, & Dubois-Comtois, 2005; O'Connor & Croft, 2001; Spieker & Crittenden, 2010); insecure attachment rates are higher among preschoolers with disruptive behavior disorders or those with depressed mothers (i.e., 80–87%; Greenberg, Speltz, Deklyen, & Endriga, 1991; Teti, Gelfand, Messinger, & Isabella, 1995). Dyadic attachment quality during preschool is a significant predictor of later social–emotional health. For example, research demonstrates associations between secure attachment patterns during preschool and positive affect, social competence, and emotion regulation during school age (Moss, Rousseau, Parent, St-Lauren, & Saintonge, 1998; National Institute of Child Health and Human Development [NICHD] Early Child Care Research Network, 2001). To understand best how to promote early secure attachments, a large body of research has examined dyadic and environmental predictors of attachment quality. In the next section, we review findings about the effects of mental representations of relationships, maternal insightfulness and reflective functioning, maternal psychopathology, and exposure to interpersonal trauma.

PREDICTORS OF ATTACHMENT QUALITY

Relational representations constitute the cognitive and affective templates for relational experiences. Bowlby (1982) coined the term "internal working models" to describe these relational representations, which derive from everyday experiences with significant others (often, the adult's parents and romantic partners), influence the parent's perception and experience of the child's behavior (e.g., interpreting the child's crying as signal of distress, physical pain, or "bratty" behavior), and are a key contributor to the parent's ability to provide sensitive care and form a secure bond with the child (Fonagy, Steele, & Steele, 1991). Research shows that women with positive and balanced representations (i.e., cohesive, flexible, and accepting view of the child; generally attributing benign motives to the child's behavior) have more joyful, sensitive, and positive mother–infant interactions (Dollberg, Feldman, &

Keren, 2010; Slade, 1999; Rosenblum, Dayton, & McDonough, 2006), and more secure mother–child attachment relationships (Benoit, Parker, & Zeanah, 1997; Huth-Bocks, Theran, Levendosky, & Bogat, 2011; Zeanah, Benoit, Hirshberg, Barton, & Regan, 1994). On the other hand, representations of the infant as idealized or rejected, and those characterized by low affective engagement or overwhelming emotions, are associated with insecure attachment (Benoit et al., 1997; Huth-Bocks et al., 2011). Notably, these representations play a role in the intergenerational transmission of attachment patterns: Women's internal working models of their own early relationships with caregivers influence their representations of their infant (Benoit & Parker, 1994; van IJzendoorn, 1995), as well as their parenting behaviors (Cohn, Cowan, Cowan, & Pearson, 1992; Slade, 1999).

Oppenheim, Koren-Karie, and Sagi (2001) propose that maternal insightfulness is a key element of caregiving representations. Insightful parents have an emotionally complex and accepting view of the child, characterized by benign and adequate understanding of the child's behavioral motives that is updated when new, conflicting information is available. In research, insightfulness predicts more sensitive maternal behaviors and more secure infant–mother attachment, whereas parents with an inflexible view of their child (i.e., interpreting behaviors in terms of rigid, preconceived notions) are more likely to have insecurely attached children (Koren-Karie, Oppenheim, Dolev, Sher, & Etzion-Carasso, 2002; Oppenheim et al., 2001). Fonagy and Target (2005) proposed that reflective functioning (RF), a construct similar to insightfulness, is a key influence on attachment quality. RF involves the capacity to make sense of interactions by recognizing the child as having his or her own "mind" and being motivated by his or her own thoughts, feelings, wants, and needs (Fonagy & Target, 2005). A mother's RF in regard to interactions with her child is associated with more sensitive maternal behavior and secure infant–mother attachment (Meins, Fernyhough, Fradley, & Tuckey, 2001; Rosenbum, McDonough, Sameroff, & Muzik, 2008; Slade, Grienenberger, Bernbach, Levy, & Locker, 2005).

Attachment quality is negatively influenced by parental psychopathology. For example, early parent–child relationships, attachment quality during preschool, and child social–emotional well-being have all been associated with maternal depression. In their large, multisite study, Campbell and colleagues (2004) found that chronic or intermittent depressive symptoms (from birth to age 3) were associated with resistant and disorganized attachment patterns during preschool. Also, infant disorganized attachment is associated with higher levels of maternal depression in pregnancy (Hayes, Goodman, & Carlson, 2013). Importantly, across these and other studies, results suggest that there are important moderators of these associations, including the quality of parenting behavior, suggesting that sensitive caregiving may mitigate the negative effects of maternal psychopathology on attachment quality and child outcomes (Campbell et al., 2004; Goodman et al., 2011).

Traumatic experiences also pose a challenge to young children's attachment

relationships. Traumatic stress exposure is very common during early childhood, with high incidence of motor vehicle or household accidents, physical abuse or neglect, and exposure to domestic and community violence (Egger & Angold, 2004). Notably, traumatic experiences may include threat to self or a caregiver, and can distort the normative senses of danger and safety, causing intense dysregulation. Trauma exposure may lead to child temper tantrums or aggression, impulsivity, changes in sleeping or feeding, fearfulness or clinginess, and physiological arousal (Van der Kolk, 2014). Children may recreate memories of events that occurred prior to their acquisition of language but may misconstrue aspects of the trauma due to developmental understanding of cause and effect (Lieberman, Ghosh Ippen, & Van Horn, 2005). Therefore, parent sensitivity is key to assisting a young child in processing the trauma (Egger & Angold, 2004). Unfortunately, parents are often also exposed to the traumatic event, and its impact is profound, creating a relational stance of victim–victimizer or helpless bystander, or generating negative attributions about a child (e.g., as perpetrator of domestic violence; Lieberman, Ghosh Ippen, & Van Horn, 2005).

Predictors of change in attachment quality have been less frequently explored, but there is evidence of malleability (both positive and negative change) in response to contextual factors, such as income, social support, and marital satisfaction (Fish, 2004; Moss et al., 2005). Our understanding of the factors that shape attachment relationships and continued investigation of the influences that can enhance parent–child relationships or ameliorate problematic attachment patterns has informed the field of attachment-based assessment and intervention.

USING ASSESSMENT TO FRAME THERAPEUTIC INTERVENTIONS WITH PARENT–CHILD DYADS

Given the primacy of child–parent attachment in early childhood, assessment protocols that help to both identify needs and frame therapeutic interventions with parent–child dyads are clearly needed. Assessment protocols that emphasize a developmental–relational framework are likely to highlight both characteristics of the environment that contribute to the etiology of the child's problems and protective factors that can facilitate child resilience (Rosenblum, 2004). Empirically based rating scales can provide some information regarding the parenting/caregiving environment and the parent–child relationship; for example, the Devereaux Scales of Mental Disorders (Naglieri, LeBuffe, & Pfeiffer, 1994) or the Parenting Stress Index (Abidin, 1995). However, to assess child–parent relationships comprehensively, it is also necessary to consider both the quality of *observed interaction* and the characteristics of the *internal working models* of the relationship for both parent and child. Assessing the parent–child relationship is an important component of evaluation when there have been separations or disruptions in care (e.g., adoption or

foster care), when the child has experienced interpersonal trauma, or when parental psychopathology is a clear contributor to the preschooler's symptoms. Even when children bring qualities and characteristics to the environment that may uniquely explain the etiology of problematic behavior, attention to family relationships and parent–child attachment is warranted by the centrality of these domains in the young child's life. Understanding the behavioral, cognitive, and affective components of the relationship between the child and his or her parent can help identify needs to be met, in order to permit parents to support their children's optimal achievement of their full developmental and social–emotional potential.

Integrated frameworks for preschool assessment have been recommended and, increasingly, clinical programs are recognizing the need for specialized clinics for young children. To illustrate, the University of Michigan has a dedicated Infant and Early Childhood Clinic (IECC) housed within the Department of Psychiatry that incorporates an integrated developmental–relational and trauma-informed framework. Services seek both to inform understanding of child and family needs and to intervene by enhancing parent insight and capacity (Marcus, Gaggino, Rosenblum, & Shah, 2013). The clinic is an affiliate of the National Child Traumatic Stress Network and provides assessment and treatment services to all children younger than age 6 presenting in the Child Psychiatry Department.

The IECC assessment protocol not only incorporates standard diagnostic interviewing (e.g., Schedule for Affective Disorders and Schizophrenia for School-Age Children—Present and Lifetime versions [K-SADS-PL] for preschoolers; Birmaher et al., 2009; Preschool Age Psychiatric Assessment [PAPA], Egger & Angold, 2004) but also follows recommendations (e.g., Rosenblum, 2004) to incorporate evidence-based tasks to assess both observed and represented qualities of the relationship. These include observational assessment of parent–child interaction using structured interactive tasks (Crowell problem-solving procedure; Sprang & Craig, 2014), child attachment assessment via the SSP, child representation of family relationships assessed via a semistructured doll-play interview (George & Solomon, 2000; Oppenheim, 1997), assessment of parental representation of the child (Zeanah et al., 1993), and standard normed questionnaires to assess child behavior problems (Infant–Toddler Social and Emotional Assessment [ITSEA]; Carter & Briggs-Gowan, 2006; Child Behavior Checklist [CBCL]; Achenbach, 1992), social communication (Social Communication Questionnaire [SCQ]; Rutter, Bailey, & Lord, 2003) and trauma (Trauma Symptom Checklist for Young Children [TSCYC]; Briere, 2005).

These assessment activities are conducted in one day and are videotaped and reviewed by clinic staff, who then strategically selects video clips that highlight and reinforce selected parenting strengths, illustrate child challenging behavior, and show evidence of shared positive affect and delight. The parent returns 1 week later and at that time clips are shared using strategies similar to those utilized in the Insightfulness Assessment (Oppenheim &

Koren-Karie, 2002), inviting the parents (as "the expert on their child") to share their perspectives on what they think their child, and what they themselves, were thinking and feeling in each clip. The clinician uses the parents' reflections as a springboard for sharing diagnostic impressions and treatment recommendations. The goal of this approach is, ultimately, to reduce parents' feelings of shame and helplessness, enhance their sense of efficacy, and increase parental empathy for and insight regarding child and family needs.

CHARACTERISTICS AND EFFICACY OF ATTACHMENT-BASED THERAPY WITH PRESCHOOLERS

Attachment-based interventions were perhaps first developed in the context of the field of infant mental health (Fraiberg, Adelson, & Shapiro, 1975). Selma Fraiberg proposed that the mother's experiences of being cared for as a child were like "ghosts in the nursery," and shaped (or interfered with) her own ability to provide care for her child (Fraiberg et al., 1975). Thus, her parent–infant psychotherapy model focused on these representational and behavioral concomitants of poor mother–infant attachment relationships. Since then, many prevention and intervention methods have utilized an attachment perspective (Bakermans-Kranenburg, Juffer, & van IJzendoorn, 1998; Moran, Pederson, & Krupka, 2005; Steele et al., 2014) and both randomized controlled trials and meta-analytic reviews have shown that attachment-based interventions can effectively promote maternal sensitivity and secure mother–infant attachment (Bakermans-Kranenburg, van IJzendoorn, & Juffer, 2003, 2005).

Attachment-based interventions that address the difficulties of preschoolers are more recent, but a number of studies show positive outcomes for parents and their children (See Table 13.1). The goals of attachment-based therapy generally include (1) fostering more balanced caregiving representations that are coherent, flexible, open, and generally positive; (2) increasing insightfulness and RF, so that the parent can more accurately perceive their child's behavior, emotional states, and underlying motivations; (3) increasing parent sensitivity during interactions with their child; (4) enhancing the relationship or attachment quality between the parent and the child; (5) promoting child emotional and behavioral regulation; and (6) improving child social–emotional outcomes. Interventions have been implemented using individual, dyadic, group, and mixed formats (e.g., some group and some individual sessions) and delivered using a short-term (e.g., four to eight sessions; Moss et al., 2011) or long-term (20–36 sessions; Hoffman, Marvin, Cooper, & Powell, 2006; Lieberman & Van Horn, 2005) approach. Treatment protocols have been developed for substance-using mothers (Suchman et al., 2010), foster caregivers (Dozier, Higley, Albus, & Nutter, 2002), single mothers (Weihrauch, Schäfer, & Franz, 2014), adolescent mothers (Madigan, Moran, & Pederson, 2006), dyads exposed to domestic violence (Lieberman, van Horn, & Ghosh-Ippen, 2005), families reported to Child Protective Services

TABLE 13.1. Published Attachment-Based Interventions

Study	Intervention	Participants	Methods	Outcomes
Circle of Security				
Hoffman, Marvin, Cooper, & Powell (2006)	Circle of Security: 20 weekly group sessions with three co-leaders (clinicians) and video feedback	Caregiver–child dyads (11–58 months old)	Recruited from Head Start centers based on teacher rankings of family functioning ("average"); pre- and post-TX assessment	69% of disorganized at intake shifted to organized post-TX; 44% of insecure at intake shifted to secure post-TX
Cassidy, Woodhouse, Sherman, Stupica, & Lejuez (2011)	Circle of Security: Home Visit – 4: four individual home visits with video feedback	Mother–infant dyads (6–9 months old) selected for high irritability; *N* = 174 (TX *n* = 86); low income	Newborns recruited from hospital and screened for infant irritability; RCT; 12-month-old assessment control = three psychoeducation sessions	Intervention effects only for highly irritable infants (89% secure probability with intervention, 62% without)
Mom Power				
Muzik et al. (2014)[a]	Mom Power: 10 group and three individual clinician co-led sessions	Mothers and children (ages 0–6); *N* = 150; low income, trauma, depression, PTSD	Referred by health care provider (88%) or self-referred; intake and attendance data	Physical health problems and part-time or unemployment associated with increased attendance
Muzik et al. (2015)[a]	Mom Power: 10 group and three individual clinician co-led sessions	Mothers and children (ages 0–5); *N* = 80; low income and/or trauma exposed	Referred by health care provider (88%) or self-referred; pre- and post-TX assessment	Less depression, PTSD and parenting helplessness; more parenting reflective function for "completers"
Child–parent psychotherapy				
Toth, Maughan, Manly, Spagnola, & Cicchetti (2002)	Parent–preschooler psychotherapy	Mother–child dyads (*M* age = 4 years, *SD* = 6 months); *N* = 87 maltreated and 35 nonmaltreated (TX *n* = 23)	Recruited from DSS (maltreatment) or TANF recipients (no maltreatment); RCT; pre- and post-TX assessment; two controls = community standard or psychoeducation	More positive and less negative self-representations, better child relationship expectations, and less maladaptive maternal representations among TX group
Lieberman, van Horn, & Ghosh-Ippen (2005)[b]	Child–parent psychotherapy: parent–child and individual sessions (*M* = 32) with clinician	Mothers and children (ages 3–5); *N* = 65 (TX *n* = 36); dyads exposed to domestic violence	Referred by health, social work, child care, and CPS providers; RCT; pre- and post-TX assessment; control = case management + TX referrals	Less child PTSD and behavior problems post-TX; reductions in maternal avoidance symptoms

(*continued*)

TABLE 13.1. (*continued*)

Study	Intervention	Participants	Methods	Outcomes
Lieberman, Ghosh-Ippen, & Van Horn (2006)[b]	Child–parent psychotherapy	Mothers and children (ages 3–5); *N* = 50 (TX *n* = 27); dyads exposed to domestic violence	6-month follow-up of Lieberman et al. (2005); RCT; pre-, post-TX, and 6-month follow-up assessment	Less child behavior problems and maternal psychological symptoms for TX group, maintained 6 months later
Ghosh-Ippen, Harris, Van Horn, & Lieberman (2011)[b]	Child–parent psychotherapy	Mothers and children (ages 3–5); *N* = 50 (TX *n* = 27); dyads exposed to domestic violence	Reanalyses of Lieberman et al. (2006) data; classified as high (4+ events) or low (< 4 events) TSE	Among high TSE, reductions in maternal PTSD and depression, and child PTSD, depression, and behavior problems for TX group
Other interventions				
Moss et al. (2011)	Eight weekly home visits: psychoeducation, dyadic interaction, video feedback	Parent–child dyads (ages 1–5); *N* = 67 (TX *n* = 35); maltreated children	Self-referred or referred by social or CPS in Quebec due to maltreatment; RCT; pre- and post-TX assessment	Enhanced parental sensitivity, more attachment security, and less disorganization for TX group
Negrao, Pereira, Soares, & Mesman (2014)	Video-feedback intervention to promote positive parenting and sensitive discipline: six home visits	Mother–child dyads (ages 1–4); *N* = 43 (TX *n* = 22); family or parenting risk	Recruited from health and social agencies in Portugal; RCT with intake and 1-month post-TX assessment, control group = six phone calls	Enhanced mother–child interaction and family cohesion for TX group
Weihrauch, Schäfer, & Franz (2014)	Parental training for lone mothers: 20 group sessions co-led by clinicians or teachers	Mothers of children ages 4–6; *N* = 63 (TX *n* = 31); single mothers	Recruited through kindergartens in Germany, RCT with intake, post-TX, and 6-month follow-up assessment; control group = no TX	Less maternal depression, impairment, and child behavior problems for TX group; more psychological well-being for TX group, maintained 6 months later

Note. TX, treatment; RCT, randomized controlled trial; TSE, traumatic stress exposure; DSS, Department of Social Services; TANF, Temporary Assistance for Needy Families; CPS, child protective services.

[a]Analyses derived from the same sample.

[b]Analyses derived from the same sample.

for maltreatment allegations (Moss et al., 2011), and other high-risk populations (Muzik et al., 2015).

Most relational approaches to intervention emphasize the emotional connection between the parent and the child as the primary mechanism for change, as opposed to concrete behavioral skills. The theoretical rationale here is that a strong relationship that provides a "safe haven" during stressful or challenging times and promotes exploration and mastery is not dependent on specific caregiving behaviors, but rather on the general capacity of the parents to understand the needs of their child and a pattern of sensitive and contingent responses. The focus on attachment and caregiving representations, as opposed to exclusive focus on parenting behaviors, is based on two research findings: (1) that parental attachment representations moderate the effect of interventions that aim to enhance sensitivity (i.e., parent unresolved childhood attachment problems decrease benefits; Bakermans-Kranenburg et al., 1998), and (2) that continuity between a mother's history of attachment to caregivers and her attachment relationship with her infant is not completely accounted for by her caregiving behaviors (i.e., "the transmission gap"; Madigan et al., 2006).

Important components of preschool attachment-based interventions often include psychoeducation about children's attachment needs, the identification of cognitive and affective barriers to insightfulness (e.g., misattributions of child's affective states, negative affective response to a child's underlying motivation), promotion of RF, identification of parenting behaviors that are optimally responsive to the child's needs in a variety of situations, implementation of those caregiving behaviors, and continued problem-solving as parents work toward more sensitive behavior during interactions with their children. A number of specific therapeutic strategies have been reported by published studies. Many interventions include discussion of parent–child interactions and/or video feedback (Tarabulsy et al., 2008). Parents are encouraged to reflect on their child's behavior, emotions, and needs or motives, and their own behavior, emotions, and needs (Dozier et al., 2002; Moran et al., 2005). In this context, the clinician can draw attention to specific meanings assigned to the observed behaviors to modify parents' distorted perceptions of themselves and of their child, while maintaining a positive, warm, and encouraging stance (e.g., commenting on positive aspects of the observed interaction; Moss et al., 2011). Another common strategy includes in-session parent–child activities designed to support parents as they implement more sensitive parenting strategies (e.g., Muzik, Schmicker, Alfafara, Dayton, Schuster, et al., 2014). Some interventions also include discussions of a parent's own attachment history (his or her own caregivers and romantic relationships) and address additional environmental risk (e.g., marital conflict, maternal psychopathology) or promote protective influences (e.g., social support; Lieberman, Gosh Ippen, & Van Horn, 2006; Weihrauch et al., 2014). Activities and discussions are tailored to specific intervention objectives (e.g., decreasing maternal intrusiveness) and the child's developmental stage.

Some of the most commonly used treatment protocols are described below. All of these protocols have undergone some degree of efficacy evaluation and show promise to improve outcomes for young children and their parents. It is important to note that unconventional methods have been advertised as "attachment-based" (e.g., rebirth therapy) interventions, although they are not based on the empirical evidence provided by studies of early childhood attachments. These approaches have been denounced by mental health professionals and should not be used, because they are ineffective and their use is likely to lead to psychological and physical harm (Boris & Zeanah, 2005).

The Circle of Security

The Circle of Security (COS; Powell, Cooper, Hoffman, & Marvin, 2013) intervention is an attachment-focused intervention for parents of young children. The early child–parent attachment relationship provides a central foundation upon which children build self-regulatory skills and emerging social–emotional competence (Rosenblum, Dayton, & Muzik, 2009). While a number of other interventions demonstrate improvement in attachment security as an outcome, a smaller set explicitly focuses on conveying attachment concepts to parents directly. The COS provides a user-friendly, accessible, and simplified means for understanding children's attachment needs and caregiving responses, and the intervention protocols developed to deliver this content have demonstrated promising efficacy in enhancing both parent sensitivity and child attachment outcomes (Hoffman et al., 2006).

The COS intervention addresses the importance of parent sensitivity in response to two primary behavioral systems: the attachment system, which is activated in times of distress or threat, and the exploration behavioral system, which, when active, allows the child to move away from the attachment figure to explore the environment and seek new experiences (Bowlby, 1982). These two systems operate in balance: When the attachment system is active, the child seeks proximity to the parent and ceases to explore; when the exploration system is active, the "alarm bells" are quieted and the child does not need to maintain close physical proximity to the attachment figure, and can therefore venture in small but ever-increasing ways out into the world. Consistent with Bowlby's depiction of a balance between the exploration and attachment behavioral systems, the COS model teaches parents that their role is to provide critical support to the child, whether the child is in exploration or attachment mode. When children are feeling comfortable and safe, the exploration system is active. At these times, children need their parent to provide a secure base in order to support exploration. Parents provide a secure base by watching over, delighting in, helping, and enjoying their children as they explore. In contrast, when children feel vulnerable, hurt, upset, or distressed, the attachment behavioral system is activated, and at this time, children need their caregiver to provide a safe haven. In other words, caregivers who are welcoming when their children approach them. Parents can provide a safe haven by welcoming

the child and providing comfort, protection, delight, and helping the child to organize his or her feelings.

COS provides a "map" that can help parents interpret their children's needs. While children may provide clear cues about what they need, for example, crying when sad, at times children may "miscue," that is, display behavior that may convey that they do not want proximity to the parent when in actuality the attachment system is active. For example, young children may push away the mom or dad, when in actuality they need their parent to provide a welcoming, safe haven. Miscues can happen for any child but are more likely to occur in children who have developed insecure patterns of attachment with their parent, as well as those who have experienced trauma or loss in prior attachment relationships. As part of the COS curriculum, parents are supported in learning not only how to read children's cues but also how to begin to "read through" children's miscues, responding to children's underlying *need*, instead of simply following children's potentially misleading *behavioral lead*.

A related critical component of the intervention has to do with helping parents identify their own "shark music," that is, the strong feelings that may be elicited in response to expression of emotions or needs. The "shark music" may distort or obscure the parents' capacity to respond in an empathic and sensitive manner and effectively meet their child's needs (akin to how the scary background music in the movie *Jaws* helps to shape viewers' perceptions). In this way parents are helped to understand how their own experiences can shape perception, and to become more aware of their role in the "dance" between parent and child, learning to take the lead in shifting from insecure to more secure patterns of attachment.

The COS intervention has been delivered in a variety of formats, including individual and group modalities, and varying lengths of time, ranging from four to 20 weeks (Cassidy Woodhouse, Sherman, Stupica, & Lejuez, 2011; Hoffman et al., 2006). The original COS intervention was an intensive, individualized model that utilized a 20-week multifamily group format with parents of preschool-age children, and involved collecting videotape observations of parent and child interaction at baseline. Clinicians reviewed these videotapes, identifying segments that were felt to reflect critical dynamics for each dyad. The clinicians then reviewed these interaction segments with parents in the context of the group, using the COS principles to guide observations, identify cues and miscues, and reflect on the child's needs, as well as on parents' own experiences identifying and responding to their children's needs.

Since the original COS group, several adaptations have been developed. A brief, four-session, home-based adaptation of the COS group was developed to meet the needs of high-risk, low-income parents of infants. This brief intervention also utilized video feedback review with parents but was delivered individually with families in the context of home visits. More recently, an eight-session, DVD-based parent group intervention was developed, Circle of Security Parenting (COS-P), in which parents are given psychoeducation and

standardized video clips are observed to provide an opportunity for learning and reflection on both children's needs and parents' own defensive behaviors that might maintain an insecure pattern of attachment.

There is emerging evidence of the efficacy of the COS approach, particularly for high-risk infants and young children. One of the initial studies evaluating the COS intervention tested efficacy in a sample of 65 high-risk toddlers and preschoolers recruited from Head Start and Early Head Start programs (Hoffman et al., 2006). Using the original 20-week, multifamily group approach, Hoffman and colleagues conducted an open trial and reported postintervention changes toward increased attachment organization and security. Specifically, at baseline, 60% of the children were classified as disorganized, with only 25% classified disorganized at follow-up. There was a corresponding decrease in insecure attachment, with a reduction from 80% insecure at baseline to 46% at follow-up. A subsequent noncontrolled open trial of the COS intervention paired with an intensive jail-diversion program for substance-using mothers of infants similarly yielded positive findings, with improvement in child attachment and maternal sensitivity, and reduced depression in mothers who completed the 15-month intensive intervention (Cassidy et al., 2010). The only randomized controlled trial of a COS intervention for parents evaluated the 4-week COS home visitation model for treatment of economically stressed parents of infants. Results did not reveal a main effect of the intervention on infant attachment; however, a significant interaction was observed, indicating efficacy of the intervention for improving outcomes only for highly irritable infants, in contrast to mildly irritable infants, and suggesting that treatment efficacy was dependent on not only infant irritability but also maternal attachment style (Cassidy et al., 2011). Efficacy has also been examined using the intervention with child care providers. Gray (2015) conducted a quasi-experimental design trial utilizing the COS-P DVD group intervention with licensed family child care providers. Results indicated no significant changes in providers' RF associated with group participation, but they did indicate improved feelings of self-efficacy and reduced depressive symptoms among providers who completed the course, relative to a nonrandom comparison group of providers who did not.

The COS set of interventions have been widely implemented, and initial evidence is promising, though each version, including the most widely utilized COS approach, the COS-P DVD, continues to require further empirical validation. Yet, clearly, the COS has had a significant impact on the field, bringing a strong and straightforward emphasis on attachment theory to interventions for high-risk parents with preschool-age children.

Child–Parent Psychotherapy

CPP is an evidence-based treatment for young children (birth to age 5) and their parents. The treatment was designed for dyads that have experienced trauma and exhibit behavioral, attachment, or psychiatric problems. Commonly, both parents and children have experienced profound and repeated

traumatic stress, including domestic violence, bereavement and loss, accidental injury, medical trauma, and repeated parental separation. CPP provides a framework for understanding and treating trauma, and supporting the parent–child relationship within the context of a play-based developmental–relational therapy. The primary treatment goals are to restore a normal trajectory of childhood development and healthy dyadic functioning. This is supported in treatment by enhancing affect regulation, trust, mastery, and ultimately productive engagement within the environment (Lieberman & van Horn, 2005). Treatment length is variable, ranging from a few months to 12–24 months, often depending on the severity of trauma and symptomatology.

The treatment consists of assessment, foundation, intervention, and termination phases. CPP espouses an ecological–transactional model of development (Sroufe, 2005) exploring the interplay of child behavior and development within the context of the relational, family, and cultural environments in which children grow. Moreover, CPP allows parents and children to explore, understand, and repair the impact of trauma on this developmental trajectory. The treatment establishes safety at the forefront and assists parents in establishing a safe external environment to promote the child's internal sense of safety and security. Building on strengths, CPP aims to enhance parent reflective capacity by reframing misattributions fueled by the trauma history. Within this context, the therapist, parent, and child co-create the "trauma narrative"; during this process, the therapists supports the parent and child in regulating their affect and identifying physical sensations that may be embedded in the trauma. The treatment helps families to differentiate between reliving the trauma and remembering it in a more controlled and tolerable way, thus reducing the unwanted intrusion of trauma-related memories, affect, and experience in the context of daily living. The treatment also supports resilience and engagement in learning and mastery tasks by creating shared positive memories, pleasurable activities for both parent and child, and predictable prosocial and comfortable routines (Lieberman et al., 2015).

Clinicians trained in CPP develop core competencies in multiple domains. Initially, the training focuses on knowledge about trauma theory; normal development throughout the lifespan; psychopathology; and an age-appropriate, culturally informed diagnostic framework. Additional competencies include careful observation of child and parent behavior, and interacting with other agencies to support and protect the family. CPP also develops therapists' skills in the benevolent translation of child and parent behaviors to each other, and the ability to hold both the parent's and the child's perspectives throughout the treatment ("double scoop"). Reflective supervision or consultation is an essential element within CPP, allowing for exploration of countertransference, identifying the potential impact of cultural blind spots, and facilitating self-care. Clinicians' adherence to the model is assessed using fidelity measures developed for each treatment phase.

Controlled trials including infants and toddlers from a range of multicultural and socioeconomic backgrounds provide evidence that CPP can improve

both maternal and child outcomes. One randomized trial (CPP vs. community referral) included 75 dyads from multiethnic backgrounds (Lieberman, Van Horn, & Ghosh Ippen, 2005). Those children randomized to CPP showed reductions in behavioral concerns and posttraumatic stress disorder (PTSD) symptoms, while their mother's demonstrated reductions in PTSD and overall symptomatology and avoidance (Lieberman et al., 2005). A follow-up study suggests lasting effects of CPP with respect to children's behavior problems and mothers' general distress 6 months and 1 year after treatment (Lieberman et al., 2006). CPP also reduces depressive symptoms and other child behavioral problems.

Mom Power

Mom Power is a 13-session, attachment-based and trauma-informed multifamily group preventive intervention. It was designed to create a safe entry into care and to strengthen protective factors for families with young children (Muzik et al., 2015). Parents who have experienced trauma and adversity may be more reluctant to take advantage of existing services, which may be due to concrete barriers such as lack of child care or transportation, as well as trauma-related psychological variables such as shame, mistrust, or a perception that others are "hostile or unhelpful at best" (Muzik et al., 2013). Increasing attention is being paid to the need to identify effective engagement strategies, particularly for high-risk parents with young children, and to the need for a trauma-informed lens in work with vulnerable families. In response to this need, the Mom Power intervention was developed to address five core pillars designed to strengthen protective factors and promote family resilience. These pillars include (1) attachment-based parenting education, (2) enhancement of social support, (3) promotion of parent self-care and stress reduction, (4) connecting parents and children to ongoing care, and (5) support of positive parent–child interaction.

Mom Power provides a manualized parent-group and corresponding child-group curriculum. To enhance positive parenting, the intervention provides an engaging, interactive curriculum that emphasizes a child's need for a parent who can provide a secure base and safe haven, and support the child securely not only to form strong relationship roots but also to be able to branch out, explore, and grow. Social support is built through the multifamily group environment, sharing a meal, and bringing a parenting partner into the group at a later session to enhance "buy-in" and support in the real-world environment. Parents are supported in building a self-care toolkit through the introduction and in-session practice of mind–body and stress-reduction exercises each week. Each family receives individual sessions and targeted referrals to community care to address ongoing needs across a broad range of domains. Finally, the Mom Power model makes explicit use of opportunities to support child–parent interaction, particularly around separations and reunions that occur over the course of the group. Separations and reunions are acknowledged and anticipated through use of songs. During the child-group period,

while parents are in their group, children are engaged in a child-led, play-based, developmentally appropriate curriculum that emphasizes predictability, trust, and mastery opportunities (e.g., playing games like hide-and-seek that encourage mastery over feelings about separation). Parents are encouraged to reflect on the separation and reunion experience in their group and to practice new skills learned in order to meet children's needs during separation and reunion. Staff members provide real-time coaching and support, and facilitate a closing activity and circle time to encourage positive parent–child interactive routines.

Preliminary evidence indicates that Mom Power is effective in reducing maternal mental health symptoms and enhancing parenting competence. Consistent with the goals of Mom Power, positive results were particularly evident for high-risk dyads including mothers who had experienced interpersonal violence (Muzik et al., 2015). A corresponding study examined mechanisms underlying improvement. Results suggests that for high-risk mothers, participation in Mom Power is associated with increased activation of the amygdala during an functional magnetic resonance imaging (fMRI) task designed to elicit empathy by observing photos of children displaying different emotions. When asked to "feel empathy" versus "simply observe" these images, high-risk mothers had longer reaction times and showed differential activity in the right amygdala. Furthermore, high-risk mothers showed increases from pre– to post–Mom Power in this empathy task-induced amygdala activation, and increased activation in this circuitry was associated with reductions in parenting stress (Muzik, Morelen, Ho, Rosenblum, & Swain, 2015). More recently a randomized controlled trial of Mom Power delivered by community mental health providers indicates that Mom Power is effective in enhancing the security of parents' mental representations of their children (Muzik & Rosenblum, 2014). Given findings that indicate particular efficacy for parents with trauma histories, the Mom Power curriculum was adapted for use with military families with preschool-age children, called the strong military families model; this model is currently undergoing a federally funded evaluation (Rosenblum & Muzik, 2014).

CLOSING THOUGHTS: LIMITATIONS AND FUTURE DIRECTIONS

First, attachment-based interventions address the parent–child relationship as a privileged context with strong and lasting implications for children's social–emotional development. Likewise, attachment and relationally informed assessment practices have begun to be integrated into mental health services, using structured tasks and interviews that are well established in research settings, promoting understanding of the strengths and weaknesses of early dyadic connections, and helping to uncover important points of entry for therapeutic change. However, the clinical application of these practices needs further evaluation. Second, attachment-based interventions that aim to enhance maternal

insightfulness, reflective function, sensitivity, and attachment quality may provide great benefit and enhance parent and child well-being even when other concrete etiological factors have been identified (e.g., externalizing problems related to prenatal exposures, internalizing problems related to loss). Treatment outcome studies demonstrate promising efficacy for the three interventions reviewed; however, all programs need additional evaluation with strict methodology and larger samples. One randomized controlled trial (n = 75) supports immediate and sustained reductions in child PTSD and behavioral problems, as well as maternal PTSD and depression after CPP. Replication of these findings with an independent sample is needed. Two open trials of COS demonstrate significant pre- to posttreatment changes in mother–child attachment quality and maternal sensitivity, but the only randomized controlled trial to date reports efficacy only for highly irritable infants. Randomized controlled trials with a preschool population are needed. Last, evaluation of the Mom Power program is under way, but preliminary findings show promise and suggest reduced maternal depression, increased parental sense of competence, and enhanced maternal caregiving representations.

Another important next step as we refine the implementation of these assessment and intervention strategies is to understand better which dyads benefit most from relationally based approaches. Studies with mother–infant dyads have begun to explore this question: For example, researchers have identified parent states of mind with regard to attachment (as related to the relationship with their own caregivers) as a factor that can enhance (if coherent) or hinder (if problematic) response to intervention (Bosquet & Egeland, 2001; Moran et al., 2005), and two studies indicate that infants and toddlers with high levels of irritability (Cassidy et al., 2011) or a specific genetic polymorphism that has been linked to externalizing disorders (dopamine receptor *DRD4* genetic polymorphism; Bakermans-Kranenburg, van IJzendoorn, Piljman, Mesman, & Juffer, 2008) benefited most from intervention. Research on moderators of treatment effectiveness with preschool populations is lacking, as is research that evaluates which young children may be best served through a relationally oriented treatment (vs. other empirically based treatment modalities).

Another significant direction within the development, evaluation, and dissemination of attachment-based assessment and treatment methods is the integration of cultural factors. A great deal of our theoretical framework for the relationships between child adjustment and attachment, relationship representations, and caregiving sensitivity was developed through observation and testing of white mother–child dyads. Mesman, van IJzendoorn, and Bakermans-Kranenburg's (2012) systematic review supported the strong influence of parental sensitivity on child development among ethnic/minority families, but they also conclude that socioeconomic stress has a very negative impact on caregiving behaviors, and interventions should jointly address contextual and caregiving factors. Notably, two of the interventions reviewed earlier have been evaluated with families from minority ethnic backgrounds and/or living in poverty (i.e., Mom Power, CPP), and one of them is successfully used with monolingual Spanish-speaking families. However, as the United States

becomes increasingly culturally and linguistically diverse, mental health professionals need to understand better how cultural values influence participation and benefit from these interventions.

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14

Updates on Early Interventions for Autism Spectrum Disorder

Timing, Targets, and Mechanisms

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Autism spectrum disorder (ASD) is a group of neurodevelopmental disorders that require lifelong care and support. With advances in intervention science, improved outcomes have resulted in fewer children entering school as nonverbal (Tager-Flusberg & Kasari, 2013), more children educated in mainstream settings (U.S. Department of Education, 2013), and greater numbers of children with optimal outcomes, defined as no longer meeting ASD diagnostic criteria (Fein et al., 2013; Centers for Disease Control and Prevention, 2014). These findings have led to intense lobbying for intensive interventions by parents and professionals, with the result that insurance companies now reimburse for behavioral interventions and consider them medically necessary in nearly half of the states in the United States (Centers for Medicare and Medicaid Services, 2011). Scientists, too, have been swept up by media enthusiasm for results, suggesting that we are on the verge of a "cure" for primordial infants with ASD and that children can shed their diagnosis to become cases with "optimal outcome," if they receive intensive early intervention (Fein et al., 2013).

In contrast to the widespread community belief in the benefits of early intervention, several commissioned reviews of the literature conclude that the evidence supporting early interventions is "insufficient to low" when rigorous

scientific studies are considered (Warren et al., 2011; Maglione, Gans, Das, Timbie, & Kasari, 2012). Given the marketplace mandate for early behavioral interventions, the current evidence base requires renewed scrutiny in order to make informed recommendations and to consider why and when interventions are needed. Additionally, the growing neurodiversity movement (largely comprising individuals who identify themselves as being on the autism spectrum) questions the underlying premise of several interventions that aim to cure, or "normalize," behaviors of children with ASD (Kapp, Gillespie-Lynch, Sherman, & Hutman, 2013). These perspectives, coupled with parents' desire for specific interventions for their children, need consideration in today's market climate.

In this chapter, we focus on the recent advancements in early interventions for young children with ASD. Taking a historical perspective, we briefly highlight the progress in the field and focus on current trends, including the influence of developmental theory on traditional behavioral techniques, which has led to the formation of a similar group of interventions called *naturalistic developmental behavioral interventions* (Schreibman, Dawson, Stahmer, Landa, Rogers, et al., 2015). We also address the following questions and resulting areas of study in the field:

1. Is there one superior early intervention approach?
2. What is the extent to which parents can augment current interventions?
3. What is the sensitivity to change of our current outcome measures?
4. Can we identify and measure mechanisms by which interventions may be providing benefit?

Answers to these questions, through rigorous, hypothesis-driven studies, will facilitate the ultimate goal of precision in the treatment of children within the heterogeneous spectrum of this disorder.

UPDATE ON THE EVIDENCE FOR EARLY INTERVENTIONS

The field of autism research has undergone a transformation in the years since the first children with ASD were described by child psychiatrist Leo Kanner (1943). Whereas it once was believed that these children were unlikely ever to respond to treatment, contemporary research has demonstrated a range of positive outcomes in cognition, language, social communication, and adaptive functioning, and has fueled the field to push for more aggressive early detection, access to higher-quality behavioral interventions, and a better understanding of the etiology of this complex disorder.

Modern-day interventions for ASD range from very structured models involving hours of 1:1 therapy per week, to more naturalistic developmental, behavioral interventions that are mediated through therapists, parents, and

teachers (Schreibman et al., 2015). Nearly all of these models rely on a theoretical model of intervention anchored in applied behavior analysis (ABA). A classic definition of ABA is "the process of systematically applying interventions based upon the principles of learning theory to improve socially significant behaviors to a meaningful degree, and to demonstrate that the interventions employed are responsible for the improvement in behavior" (Baer, Wolf, & Risley, 1968, p. 91). "Learning theory" refers to a number of different strategies used to change behavior in meaningful ways (e.g., the use of reinforcement to increase desirable behaviors or to reduce undesirable behaviors). The strategies employed are expected to have real-world applications and meaning.

ABA was founded on the principles of operant learning, which were applied to children with ASD as early as the 1960s and 1970s. The most influential early work was that of Ivar Lovaas (1987), who demonstrated large gains in measures of intellectual functioning and school placement for children who received 40 hours per week of a form of ABA called "discrete trial training" (DTT). DTT is grounded in the theory that children with ASD have difficulty learning from the natural environment; therefore, Lovaas and his successors teach by breaking down tasks into small steps and applying reinforcement, often in the form of edibles, when a task is completed. After Lovaas's groundbreaking work showing that children with ASD could make significant improvements, DTT quickly gained popularity, with many parents demanding 40 hours per week of the therapy for their children, but the method was not free of shortcomings. In fact, further study showed that DTT did little to help children generalize their learned skills to new surroundings and could also lead to more challenging behaviors and overreliance on the prompts (Schreibman et al., 2015). These findings led researchers to question some of the traditional techniques and to make room for new ones to emerge.

Like more traditional methods of treatment for children with ASD, most naturalistic developmental behavioral interventions (NDBIs) are firmly rooted in the principles of ABA and meet all the criteria for such practices, including an emphasis on operant teaching principles and careful measurement of socially significant outcomes (Baer et al., 1968). Some of the key characteristics of NDBIs include teaching in natural contexts (e.g., through play and daily routines), using child-led practices, and utilizing natural contingencies in the environment (Schreibman et al., 2015). Although these practices may seem commonplace in the treatment literature now, they reflect a radical shift in the treatment methods used for young children with ASD. The reliance on teaching in natural settings, using contingent and natural reinforcement, and allowing the child to initiate and lead the interaction addresses the concerns raised by traditional ABA approaches by emphasizing developmental principles and applying what we know regarding how typical children learn.

Precipitating this shift was a growing awareness of the "core" features of autism and what is truly unique to the disorder. Foundational work by Marian Sigman and colleagues showed that young children with ASD could be reliably distinguished from typically developing and developmentally

delayed children by their difficulties in joint attention, or the triadic initiation of shared attention between the child, another person and an object of interest, and their difficulties engaging in symbolic representation or pretend play (Kasari, Sigman, Mundy, & Yirmiya, 1990; Mundy, Sigman, Ungerer, & Sherman, 1987; Sigman, Ungerer, Mundy, & Sherman, 1987). These pivotal studies demonstrated that early difficulties in nonverbal social communication were a hallmark of the disorder and should be a focus of early intervention.

The "evidence" for early interventions has also increased dramatically in the past few years. While, traditionally, there were few well-designed, rigorous tests of these interventions, study designs have improved to such a degree that we are seeing an explosion of randomized controlled clinical trials. Randomized designs represent an improvement over previous designs, because they protect against biased and spurious results. Improvements in study design now include larger sample sizes, replication studies, and studies that employ comparative intervention designs.

In recent years, new studies on early interventions have converged, allowing us to better address controversies in the intervention literature, including whether only one ABA-based intervention (e.g., DTT) is effective, whether parents can effectively expand intervention outcomes with their children, and whether interventions are addressing meaningful outcomes. Newer work also reflects the growing need to disseminate empirically validated interventions into community, schools, and homes, and especially to address the needs of families in underserved minority groups.

A SINGLE BEST TREATMENT APPROACH DOES NOT EXIST

A major question in the intervention literature has been whether there is only one effective type of ABA intervention. In the original study, Lovaas (1987) suggested that 40 hours of the comprehensive ABA approach, DTT, over 2 years was effective for increasing IQ and normalizing children so that they could enter school without detectable signs of ASD. The Lovaas study was highly criticized for lack of rigorous testing, specifically with regard to lack of randomization. While no studies have compared DTT to another intervention, there is mounting evidence that several comprehensive treatment models obtain similar gain in IQ points as the Lovaas study. In randomized controlled trials, both Smith, Groen, and Wynn (2000), who conducted a replication study of the Lovaas (1987) study, and Dawson et al. (2010), who tested an NDBI with a combination of behavioral and developmental strategies (Early Start Denver Model [ESDM]) obtained similar increases in IQ over 2 years with 20+ hours per week of individualized therapy. Both therapies obtained a difference of about 10–15 IQ points in the experimental treatment groups versus the control groups, which were receiving far less therapeutic intervention. Other intervention studies have obtained similar increases in IQ points over time, with overall gains in IQ across a variety of intervention types (Sallows

& Graupner, 2005; Landa, Holman, O'Neill, & Stuart, 2011; Kasari, Siller, Huynh, Shih, Swanson, et al., 2014). Thus, it does not appear that any particular intervention is associated with greater effect on IQ; rather, interventions generally may produce increases over time at a minimum dose of individualized intervention (10–20 hours per week).

What is not clear from studies that have focused on the primary outcome of IQ is which, if any, intervention techniques are more effective in treating the core social communication features of the disorder. Comprehensive treatments may address social communication impairment, but not assess whether it improves as a result of treatment. Targeted treatments, on the other hand, may directly teach and assess improvement on core social communication impairment. These studies have reported improved outcomes. The earliest randomized controlled trial (RCT) examining differences in core deficit domains of joint attention and symbolic play found that children who received either treatment in conjunction with a traditional 30-hour-per-week ABA program made substantial gains in the respective domains, and that these gains related to larger language gains 1 year later compared to a control group that received traditional ABA only (Kasari, Freeman, & Paparella, 2006; Kasari, Paparella, Freeman, & Jahromi, 2008). Other researchers have found that children with ASD can learn to engage in more imitation with eye contact after a classroom-based intervention (Landa et al., 2011).

PARENT-MEDIATED INTERVENTIONS CAN OFFER BENEFITS

New emphasis has been placed on parent-mediated interventions, in part due to greater confidence in the ability to identify children with ASD at younger ages, and because parents are viewed as essential in helping to generalize therapeutic gains to the home and community. Parent-mediated interventions tend to be low dose (an hour long and one to three sessions per week) over short periods of time (8–12 weeks), although some have been of longer duration (9–12 months; Green et al., 2010; Wetherby et al., 2014). Outcomes have been variable. Three recent studies demonstrated significant benefit for both parents and children when comparing an experimental intervention to an active comparator, a significant design improvement over previous no-treatment control groups (Kasari, Lawton, Shih, Barker, Landa, et al., 2014; Kasari, Gulsrud, Paparella, Hellemann, & Berry, 2015; Wetherby et al., 2014). All three studies are NDBIs (Schreibman et al., 2015). Two are based on joint attention, symbolic play, engagement, and regulation (JASPER), a social communication module derived from the previously described joint attention and play study (Kasari, Freeman, & Paparella, 2006; Kasari, Paparella, Freeman, & Jahromi, 2008) that targets core social communication areas of development and finds consistent improvement in these outcomes. One study compared 24 home sessions of parent-mediated hands-on coaching of JASPER to a group-based parent education model with 112 low-resource preschoolers

and caregivers across five sites (Kasari, Lawton, et al., 2014). Results indicated significant improvement in parent–child joint engagement, child initiations of joint attention, and symbolic play over 3 months that maintained over a 3-month follow-up. These outcomes align with some of the core social communication impairments observed in young children with ASD. Joint engagement requires active participation of both partners: It is not enough that the parent is attentive to the child; the child must also play an active role. "Joint attention" refers to verbal and nonverbal skills that are used to direct or share attention with a partner, such as pointing to something of interest or showing a toy to the person. Symbolic play, a more advanced level of play than functional play, requires imagination. While these core symptoms appear improved in the short term (over 6 months), it will be important for future studies to examine the downstream effects of these early interventions on later development of language and cognition.

Two other recent studies focused on intervention for toddlers and caregivers, with one demonstrating significant gains in child receptive language and social communication skills over 9 months and based on the SCERTS (social communication, emotion regulation, and transactional supports) model of early intervention (Wetherby et al., 2014), and the other (based on JASPER) finding improvement in joint engagement, diversity of play, and generalization to the child's engagement with his or her teacher across 3 months of intervention that maintained to a 6-month follow-up (Kasari et al., 2015). These studies are consistent with earlier studies demonstrating the benefits of parent-mediated interventions on both child and parent outcomes when compared to no-treatment control groups (Green et al., 2010; Kasari, Gulsrud, Wong, Kwon, & Locke, 2010).

In contrast, some studies found significant increases in parent responsiveness but not in child outcomes (Kasari, Siller, et al., 2014), while others found that child effects were significant for only a smaller subgroup of children (Carter et al., 2011; Siller, Reyes, Hotez, Hutman, & Sigman, 2014). Still other studies found no apparent benefit to parents or to children (Rogers et al., 2012). There are a number of possible explanations for these mixed results. First, parents may not incorporate strategies into their daily routines because they have not sufficiently bought into the intervention. "Buy-in," or belief in the treatment, may be especially sensitive to parents' ability to see change in their children's behaviors and strategies they can easily implement at home (Kasari et al., 2010; Kasari, Lawton, et al., 2014). Second, the outcome measure itself may not be sensitive to change, or it may be too far removed from the treatment content. It also is possible that some treatments may not be more effective than the strategies already being used by parents or community service providers. Finally, other factors that may affect effectiveness include age of child, parental stress, and other family characteristics that may yield low fit between family and intervention. In other words, the variability in effectiveness of different interventions cannot be explained by one unifying cause.

OUTCOMES OF INTERVENTION STUDIES NEED SCRUTINY

The metric used for determining treatment effectiveness has been a topic of great interest over the last several years (Anagnostou et al., 2015). The goal of outcomes research is the identification of a meaningful outcome, with increasing attention to "core deficits" (defined as particular behaviors that appear core to the syndrome and cause significant impairment). Most comprehensive treatments examine change in IQ, a measure of cognition that is not considered a core deficit, since the majority of individuals with ASD function within the typical range of IQ. Measures of IQ tend to be unstable in young children, and nonspecific intervention approaches tend to increase IQ scores. Moreover, change in IQ may not reflect more robust or foundational changes in core social communication domains (e.g., play).

Two other potential confounds in outcome data include the identity of the reporter and whether the measures result from prompted interactions or responses. For example, some studies involve parents in the intervention, and the outcomes rely on parent report, which may be biased because of the parents' involvement (Wood et al., 2009, 2012; Laugeson, Frankel, Gantman, Dillon, & Mogil, 2012). It may be difficult to determine outcome if the parents report benefit for their child, but the children themselves may not report or demonstrate change. In other studies, the outcome may be a prompted response by the child (Ingersoll, 2011; Hardan et al., 2015). Prompting a response may be an important strategy to teach children, but the ultimate goal of intervention should be an outcome that reflects spontaneous initiations and generalization to gauge the extent to which children have learned. Finally, because outcomes are most commonly examined over relatively short periods of time, long-term benefits have yet to be rigorously tested.

WHEN ARE INTERVENTIONS NOT INDICATED?

One finding that surprises many intervention scientists is that not all children require the intervention under consideration. For example, some children will likely make improvements with exposure to the usual schooling experiences of young children. A study of children's peer-related engagement on their school playground found that about 20% of children assessed for a recess peer-engagement intervention were already engaged with their peers 80% of the time before intervention even began (Shih, Patterson, & Kasari, 2014). This percentage of engagement was the same level at which their typical peers were playing, which suggests that there was little need for additional intervention targeting peer engagement.

There are other indications that participants themselves may not desire interventions (Bolte, 2014). Individuals who can opt into interventions often do not (Kapp et al., 2013) based on many personal beliefs. In studies of prodromal autism, 20–40% of parents of eligible infants refuse to participate

(Green et al., 2010; Rogers et al., 2014). These findings suggest that there are many potential influences and competing demands in the lives of those with ASD and their families.

INTERVENTIONS CAN BE PERSONALIZED

Recognizing that one size does not fit all, researchers may also be better served by employing more rigorous treatment designs that can systematically build personalized interventions. These types of designs involve the tailoring of interventions to provide treatment at critical times in a child's development. In a recently published adaptive treatment study for children with ASD, a sequential multiple-assignment randomized trial (SMART) design was applied to treatments targeting 5- to 8-year-old, minimally verbal children with ASD (Kasari, Kaiser, et al., 2014). In this study, children received a social communication and language intervention with or without the addition of an augmentative and alternative communication device (AAC; e.g., iPad with speech-generating software). Based on predetermined metrics for response, if the child was deemed to make minimal gains during the initial study period, the treatment was augmented with increased dose, or the addition of the AAC device, if not already present. Results indicated that beginning treatment with the AAC was superior to all other adaptations for spontaneously produced, socially related spoken language. These findings suggest that a pivotal component to this social communication intervention is the presence of the AAC device. The design used in this study bodes well for future studies that aim to better understand the direct effects of different intervention components and to better personalize interventions.

MOVING EMPIRICALLY SUPPORTED INTERVENTION INTO COMMUNITY SETTINGS

With a growing number of treatments being made available to families, the task of deployment into the community must also be addressed. One reasonable place for these interventions to take place is within the school system. Children of school age spend an average of 30 hours per week receiving education, and children with ASD are no different. It stands to reason that the research into best practices should be implemented in these settings. Several models have been created for use in classroom settings. Research conducted in 2013 evaluated the effectiveness of several classroom programs, including the Treatment and Education of Autistic and Related Communication-Handicapped Children (TEACCH) model, which centers on adapting the environment to the individual needs of the child and includes the use of visual schedules and structured activities; Learning Experiences: An Alternative Program for Preschoolers and Parents (LEAP), an inclusive preschool program that integrates children with ASD into the mainstream education classroom; and

high-quality programs that do not prescribe to a specific philosophy. In all three settings, children made significant gains in communication, motor, and reduced autism symptomatology, which suggests that gains at similar rates can be made in high-quality programs regardless of the exact methods used (Boyd, Hume, Mcbee, Alessandri, Gutierrez, et al., 2013).

Other researchers have looked at adapting and deploying empirically supported practices for the school setting. For example, the JASPER intervention has been adapted for the classroom setting, and preliminary results are positive for child engagement and play, and teacher fidelity to protocol (Chang, Shire, Shih, & Kasari, 2016; Lawton & Kasari, 2011). The school system appears to be a viable setting for conducting research and disseminating best-practice research, but this work is in its infancy and requires more rigorous study and replication.

Coupled with new work in the community is the growing awareness that not all interventions work in all communities, especially communities with few resources. It is well known that African American and Latino children experience delays in detection, diagnosis, and treatment compared to European American children (e.g., Mandell, Listerud, Levy, & Pinto-Martin, 2002; Mandell, Wiggins, Carpenter, Daniels, Diguiseppi, et al., 2009). Less is known about the factors related to this discrepancy, although research points to a complex interaction among scarce resource, lack of awareness, and cultural factors (Carr & Lord, 2013; Magana, Lopez, Aguinaga, & Morton, 2013). One way to address this concern is to partner fully with the community to address the issues head-on and develop interventions that are meaningful and sustainable together with the community members it will affect. Researchers are beginning to utilize community participatory research models to understand better the obstacles faced in the community and to create new solutions. For example, Kasari, Lawton, et al. (2014) examined a parent-training program that was designed to reach such families by offering sessions in family homes and neighborhoods at times convenient to the family, in the family's primary language, and with a focus on daily routines. Retention was high, and children who received the intervention surpassed a control group in joint attention and social engagement; however, 24% of families never initiated the intervention despite signing consent forms and indicating interest. The difficulty of engaging families beyond an initial contact suggests that even more needs to be done to engage families in the process from the beginning (Carr, Shih, Lawton, Lord, King, & Kasani, 2015). Future work on how to engage families in the process will likely contribute to more sustainable models of care in community.

BEHAVIORAL AND NEURAL MECHANISMS UNDERLYING THE EFFECTS OF INTERVENTION CAN BE QUANTIFIED

We have highlighted the considerable variability in outcomes with intervention, explaining that some of this variability results from heterogeneity in the

target population, in the nature of interventions being used, and in the choice of outcome measures. As we begin to document the behavioral outcomes of specific interventions and to understand differences in response to treatments, we need to have a better understanding of both the behavioral and biological mechanisms underlying the effects of treatment. In other words, we know that interventions can modify behavior, but which behaviors are most sensitive to change? Is there an underlying biological change that is associated with that behavior and, if so, does the nature of this change inform our understanding of the way in which the intervention actually works?

First, in terms of behaviors, researchers' have begun to isolate components of behavioral interventions in the hope that better understanding *how* these approaches work can inform further treatment development. The term "active ingredients" has become popular in recent years, calling attention to the fact that we know very little about the relationship between a packaged and multifaceted behavioral intervention and a child's outcome. One way to test this relationship is to apply statistical mediation analysis. Two studies to date that have done this in regard to behavioral intervention in ASD found that two key strategies seem to impact the social interaction between child and parent. In the Preschool Autism Communication Trial (PACT), an RCT examining the effects of a targeted parent–child interaction intervention in the United Kingdom, parental synchronized communicative acts mediated the relationship between treatment and rating of autism symptomatology (Aldred, Green, Emsley, & McConachie, 2012). In a similar, parent-mediated intervention, this time employing the targeted JASPER intervention, parent's use of imitative and elaborative play strategies was a key mediator of treatment gains in joint engagement (Gulsrud, Hellemann, Shire, & Kasari, 2015). While both studies reported interventions that comprised many strategies and facets, these isolated components were most directly related to the gains in the primary outcome. These studies inform the field of the underlying pathway of change in children with ASD, calling attention to the most critical aspects of the intervention for future study and implementation.

Researchers also have begun to investigate biological measures of treatment response, with emphasis on functional imaging methods that can capture changes in brain function with exquisite temporal resolution (on the order of milliseconds). Two primary methods of interest have included electroencephalography (EEG) and magnetoencephalography (MEG) (Jeste, Frohlich, & Loo, 2015; Port et al., 2015). Both EEG and MEG measure neuronal activity with exquisite temporal resolution, and they can quantify change in neuronal oscillations and synchrony that can occur within milliseconds. Such physiological change can precede behavior or, sometimes, may occur despite stability in, or absence of, a behavior. In the latter event, it may be that the behavior being measured was too crude an indicator of the change that had truly taken place, or that other factors, such as the child's overall cognitive or motor ability, masked the behavioral change that can be identified.

Two types of neurophysiological domains have been studied with regard to treatment outcomes: event-related activity (which serves as a measure of perception and cognition) and spontaneous patterns (sometimes referred to as "resting state") that may relate to cortical connectivity or function. Event-related neurophysiological studies have focused mostly on face perception as a domain central to the developmental of social cognition. There exist considerable normative data on the development of face perception, with neural correlates of attention to and recognition of faces well established in early infancy (de Haan & Nelson, 1999). Moreover, atypical face perception has been linked to core deficits in ASD (for review, see Jeste & Nelson, 2009) and in early risk markers in infant siblings of children with ASD (Tierney, 2011). In a study of toddlers with ASD undergoing a behavioral intervention known as ESDM, investigators asked whether EEG oscillatory activity in response to faces "normalized" after intervention. While the study design was limited by lack of preintervention EEG assessments, the investigators found that toddlers receiving the intervention demonstrated greater "activation" when viewing faces, similar to typically developing toddlers, and in contrast to those toddlers receiving standard community services. This activation pattern correlated with improvements in social behavior. In a more recent study of preschoolers undergoing pivotal response treatment (PRT), Pelphrey and Carter (2008) used fMRI to characterize activation in social brain networks with treatment. They found that baseline activation patterns (hypo- vs. hyperactivation of the superior temporal sulcus [STS]) correlated with the specific brain changes found with treatment. Specifically, those with hypoactivation of the STS prior to treatment demonstrated increased activation in reward circuitry, while those with hyperactivation in the STS demonstrated decreased activation in salience networks. Although based on a small sample size of 10 children with ASD, and without a nonintervention control group, these findings reinforce the utility of functional brain measures to identify baseline features that may not only guide choice of treatment but also may help explain the neural mechanisms by which the intervention may be working (Ventola et al., 2015). Finally, in a study of adolescents enrolled in a social skills intervention (Program for the Education and Enrichment of Relational Skills [PEERS]), investigators found that children who completed PEERS showed a shift from right to left dominance in the gamma band, with improvement in social behavior related to degree of left-hemisphere gamma dominance.

Research in biological mechanisms, while promising, is still in its infancy, with small and heterogeneous samples limiting the generalizability of findings. Future studies will need to systematically measure and compare the change in neurophysiological patterns between different interventions, then relate this change to behavioral or developmental changes before and after an intervention. It is likely that specific patterns of change relate to improved outcomes and, furthermore, that baseline characteristics may help stratify children based on the likelihood of response to particular interventions. However,

to understand how biomarkers may be related to intervention response, biomarkers must be tested as rigorously as behavioral measures in order to provide valid information. We might expect that in the future, interventions will need to be rooted in neural mechanisms in order to facilitate more targeted approaches to the goal of improved outcomes.

CONCLUSIONS AND CONSIDERATIONS FOR THE FUTURE

The field of intervention research has evolved from descriptive studies with small samples to clinical trials that employ more rigorous methods in baseline assessments, outcome monitoring, and inclusion of comparison groups. Current evidence suggests that several interventions are available that can improve outcomes for children with ASD and their families. However, the science of intervention requires more precision, both in the targets of treatment and the key components of the treatment that can affect change. We need to test strategically the core elements of each intervention to determine which components are necessary for the success of the intervention; conversely, we need to identify the core features of a child that require intervention, and that may be most amenable to treatment. Precision will also require the identification of quantitative biomarkers that relate to the mechanism of action of the intervention, and that can be monitored with behavior as a marker of treatment response. The overarching goal in intervention research is the development of evidence-based interventions that embrace the individual and the unique features of a child, while implementing strategies that converge on the common impairments in social communication skills that define ASD.

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15

Updates on Preschool Psychopharmacological Treatment

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In recent decades, our field has witnessed substantial advances in early childhood mental health and in psychiatric treatment of young children. These advances converge in the area of preschool psychopharmacological treatment. In the areas of early childhood mental health, rigorous work featured throughout this handbook highlights the prevalence and validity of psychiatric disorders in young children; a growing understanding of the complex associations among biological, caregiving, and social contexts that shape early childhood mental health; and effective treatment approaches to reduce suffering and improve the long-term developmental course. In the world of child psychopharmacological treatment, pediatric indications for psychopharmacological agents continue to grow, with new treatments and expanded indications, and a growing appreciation of the developmental issues specific to pediatrics in psychopharmacological treatment.

At the intersection of these worlds sits the topic of early childhood psychopharmacological treatment. This chapter reviews the trends in prescribing practices; briefly addresses the developmentally specific issues of assessment, diagnosis, and pharmacological regulatory processes; presents existing data related to preschool psychiatric disorders; and concludes with a discussion of policies to further early childhood well-being in the area of preschool psychopharmacological treatment.

YOUNG CHILDREN: A SPECIAL GROUP

Considering psychopharmacological treatment in young children requires consideration of their developmentally unique patterns and needs. First, as in every treatment approach, it is critical that the diagnosis and case formulation are well-informed by multiple reporters and modes of assessment to guide an effective treatment plan. Some prescribing clinicians may not have the training or time to complete the full assessment independently, and work within a team approach for the evaluation and treatment planning, and others have the privilege of working in a team as a matter of course. Second, as detailed in this chapter, the first-line and foundational treatment for every clinical syndrome is psychotherapy. The growing array of evidence-based treatments for preschoolers reviewed in detail in this volume offers the potential for effective symptom reduction and durable treatment outcomes. Unfortunately, access to these treatments is low (e.g., Visser, 2014) due to limited dissemination beyond academic or urban centers, limited or arduous access through insurance, and conflicts in family and clinician schedules, as well as stigma and other family factors.

A child's developing brain offers a unique context for considering psychopharmacological treatment. The early years of life offer promise for effective, long-lasting interventions because of the rapid brain development and the potential for influencing the developmental trajectory. However, the lack of knowledge about the influence of psychopharmacological agents on the developing brain continues to be a driving factor in strong reactions among both professionals and laypeople to the theoretical use of psychopharmacological agents in young children. Despite the strong opinions, limited rigorous data inform our understanding of whether those long-term effects are neuroprotective or potentially neurodevelopmentally adverse. Animal models suggest long-term influence on brain development with early exposure to medications. For example, prenatal exposure to methylphenidate is associated with altered presynaptic dopamine makers in the striatum, and increased dopaminergic activity in the mesolimbic pathway in adult rats (Lepelletier et al., 2014). Prenatal exposure to selective serotonin reuptake inhibitors (SSRIs) in animals has been associated with alterations in serotonin transporter, alpha agonist, and dopaminergic receptors, as well as a range of adverse outcomes in behavior and learning in multiple studies (Bourke, Stowe, & Owens, 2014). The clinical meaning of these neurologic changes detected in animals remains unclear. However, data examining prenatal exposure to SSRIs in humans are generally reassuring with respect to measurable outcomes of overall development and early mental health outcomes (Oberlander et al., 2007).

Last, regulatory patterns shape prescribing, if only though relative neglect of this age group. Since the Best Pharmaceuticals Act for Children was passed in 2002 to promote developmentally specific psychopharmacological indications for children, only one psychotropic medication has received an

indication in the preschool age group: risperidone for children age 5 and older with autism and irritability and aggression (U.S. Food and Drug Administration [FDA], 2002). FDA indications, which are in part driven by pharmaceutical companies' request for indications, are distinctly out of sync with data in the preschool group (see Table 15.1). Many of the medications with approval in this age group are not recommended for clinical use, including haloperidol, with a historical indication down to age 3 years, and chlorpromazine, which has a historical indication down to 6 months. Additionally, methylphenidate, which has the strongest empirical support in preschoolers, carries an explicit warning against use in preschoolers, whereas mixed amphetamine salts carry an FDA indication based on historic approval for D-amphetamine.

PRESCRIBING PRACTICES

Most studies of prescribing practices focus on claims data from public or private datasets. A recent report, which included privately and publicly insured 2- to 5-year-olds described significant variation in rates of psychopharmacological agents being prescribed in outpatient visits between 1994 and 2009, although the rates in 1994 and 2009 did not differ significantly from each other, with slightly over 1% of outpatient visits resulting in a prescription (Chirdkiatgumchai et al., 2013). The rates of prescriptions rose consistently

TABLE 15.1. Currently Marketed Psychiatric Medications for Preschoolers

Medication	Brand name(s)	Approved daily dosage range	Indication	Approved ages for preschool indication
Amphetamine/ dextroamphetamine	Adderall	2.5–40 mg	ADHD	ADHD: ≥ 3 years
Amphetamine/ dextroamphetamine ER	Adderall XR	5–30 mg	ADHD	ADHD: 6– adult
Dextroamphetamine	ProCentra	2.5–40 mg	ADHD (narcolepsy)	ADHD: ≥ 3 years
Dextroamphetamine ER*	Dexedrine Spansules	5–40 mg	ADHD (narcolepsy)	ADHD: 6–16 years
Risperidone	Risperdal	0.5–3 mg	Irritability associated with autism, bipolar mania (children-adolescents), schizophrenia (adolescents)	Irritability/ autism: 5–17 years

Note. ER, extended release. Data from *www.accessdata.fda.gov*.

from 1998 to a peak of over 2% of outpatient visits in 2004, before declining again. During the same period, rates of documented mental health diagnoses rose steadily, with a 56% increase over the 15-year period, indicating that factors other than simple diagnosis drive prescribing. In fact, the rate of prescriptions relative to diagnoses decreased steadily, from 43.4 to 29.2%, suggesting that an increasing number of children who have been diagnosed with a mental health problem are not receiving psychopharmacological treatment. Whether this indicates that they are receiving evidence-supported treatment or no treatment is an important question. The prescribing patterns over time may reflect any number of medical, political, regulatory, and cultural factors. Two events are particularly interesting to consider. First, rates increased concurrently with discussion of and enactment of the No Child Left Behind legislation of 2001, which resulted in attention to even young children's standardized test performance. Similarly, it seems reasonable to wonder whether the FDA's black-box warning on SSRIs in 2004 influenced the decline in prescribing rates after that year. It is also worth wondering whether efforts to disseminate effective treatments for children, such as parent–child interaction therapy (PCIT International), the Incredible Years Series, Triple P, and Child–Parent Psychotherapy in the last decade may also play a role in the decline in rates of psychopharmacological treatment in children with psychopathology (*pcit.org*; *incredibleyearsseries.org*; *triplep.org*).

Trends within subgroups are notable. For example, children on public assistance, and especially those in foster care and on Social Security Disability, receive prescriptions at much higher rates than privately insured children (Chirdkiatgumchai et al., 2013; dosReis et al., 2014; Zito, Burcu, Ibe, Safer, & Magder, 2013). Despite epidemiological data that reveal limited gender differences in rates of disorders in preschoolers, boys consistently receive psychopharmacological treatment at rates nearly twice that of girls, even in children with a behavioral diagnosis (Chirdkiatgumchai et al., 2013). White preschoolers tend to receive prescriptions at higher rates than children of other races, although rates of atypical antipsychotic agents rose fastest for African American children in the last decade (Zito et al., 2013). Regional differences persist in the United States, with highest rates in the central region and lowest rates in the West (Visser et al., 2014; Zuvekas, Vitiello, & Norquist, 2006), and lower rates of prescriptions for preschoolers in countries other than the United States (e.g., Bachmann, Lempp, Glaeske, & Hoffmann, 2014).

Specific medication trends also differ. Stimulants remain the most frequently prescribed medications for preschoolers, followed by alpha agonists (Zito et al., 2007). While the overall rates of medications for mixed populations of publicly and privately insured children did not change substantially, rates of stimulants for preschoolers declined between 1996 and 2008 to well under 0.1% (Zuvekas & Vitiello, 2012). Conversely, in a study of publicly insured children, rates of 2- to 5-year-olds receiving atypical antipsychotic agents increased from 0.1 to 0.5% in a similar period (Zito et al., 2013), with a similar increase from 0.8 to 1.6% in privately insured children

(Olfson, Crystal, Huang, & Gerhard, 2010). Prescriber information remains limited and may vary based on local practice contexts, although primary care providers may not be the main prescribers of psychopharmacological agents for privately insured preschool patients (Gleason, Shi, & Liu, 2011; Luby, 2007).

Recently, the focus of attention has been the association of prescriptions with school policies. Specifically, preschoolers' birthdates are associated with chances of being prescribed a stimulant, with children whose birthdates are just before the prekindergarten cutoff (the youngest children in the class) having the highest rates of attention-deficit/hyperactivity disorder (ADHD) medication prescriptions (Zoëga, Valdimarsdóttir, & Hernández-Díaz, 2012).

These variations suggest that prescribing patterns may be influenced by a range of factors, including culturally informed expectations of behavior; the physical context and policy factors that influence school settings; potentially the cultural context of the family, the community, and the prescriber; and likely resource availability as well.

OVERALL APPROACH TO PSYCHOPHARMACOLOGICAL TREATMENT

In 2007, the American Academy of Child and Adolescent Psychiatry (AACAP) sponsored the Preschool Psychopharmacology Working Group to develop guidelines for prescribing for young children (Gleason et al., 2007). This group, which included early childhood clinicians and researchers, as well as psychopharmacology researchers, developed algorithms based on the empirical support for medications, the relative strength of evidence compared with alternative treatments, and clinical experience (see Figure 15.1).

The group developed principles that applied to all disorders including:

1. Consideration of medication should be preceded by an adequate trial of psychotherapy, which should continue during psychopharmacological treatment. Exceptions may be considered when a child's safety or ability to participate in normative activities (e.g., child care) are at high risk due to symptoms that may respond more quickly to a medication, but clinicians should document the rationale for such exceptions.
2. Decisions about treatment should be guided by diagnosis and level of impairment.
3. Symptoms should be tracked systematically during treatment to assess treatment effects.
4. FDA approval and level of evidence supporting treatment recommendations should guide the informed consent process.
5. Medication discontinuation trials 6–12 months after stabilization are recommended to reassess symptoms and impairment.

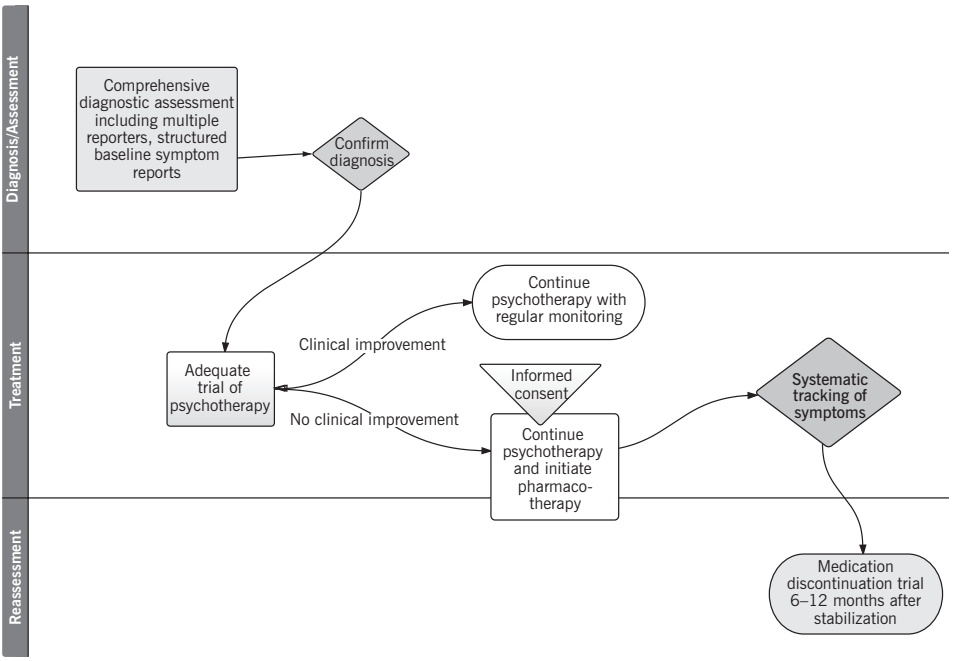

FIGURE 15.1. Approach to pharmacological treatment of preschoolers.

Attention-Deficit/Hyperactivity Disorder

ADHD is the best-studied disorder of preschoolers in terms of psychopharmacological interventions. Despite the strength of evidence for psychopharmacology in this disorder, parent management training interventions have larger or equal effect sizes and no risk of somatic adverse effects, and are proven to create more durable outcomes in children with disruptive behavior problems (Charach et al., 2011). Based on this, these interventions are considered the first-line treatment for preschool ADHD, as ADHD symptoms are included in the studied outcomes of disruptive behavior patterns.

ADHD is the most common target of psychopharmacological agents in early childhood (Zito, 2007). Among psychopharmacological treatments studied, methylphenidate (MPH) is the best researched. The Preschool ADHD Treatment Study (PATS) is the largest controlled study of any medication for preschoolers to date. The PATS was a multisite, randomized, placebo-controlled trial that evaluated the short-term efficacy and long-term safety of MPH in preschoolers ages 3 years to 5 years, 5 months. In this eight-phase trial, eligible participants completed pretreatment with parent management training prior to the MPH, with consent repeated at each step. The MPH phases included a 5-week, double-blind titration trial to identify the child's optimal dose, and a 4-week, double-blind comparison of optimal MPH dose

and placebo. MPH was more effective than placebo in treating ADHD. Optimal daily doses ranged from 7.5 to 30 mg/day, divided in three daily doses of immediate-release MPH. Treatment effects were not related to weight. The most common potential adverse effects of MPH include reduced growth rates, initial insomnia, decreased appetite, and emotional outbursts, with 11% discontinuation rate related to intolerable adverse effects (Swanson et al., 2006; Wigal et al., 2006). Comorbidity moderated treatment effects. Children with no comorbid conditions or only one comorbid disorder had a large treatment response, whereas those with two comorbid disorders showed moderate treatment responses, and those with three or more showed no treatment effects compared to placebo (Ghuman, Riddle, Vitiello, Greenhill, Chuang, et al., 2007). In the 10-month continuation phase, children continued to show improvement on the Clinical Global Impression scales. Approximately 12% of children who completed the acute treatment phase did not complete the continuation phase because of inadequate response or adverse effects.

In the long-term PATS follow-up, 207 of the original 303 participants were followed at 3, 4, and 6 years after the treatment ended, with 90% retention at Year 6. As in other samples, ADHD was highly stable in preschoolers with ADHD. Treatment outcomes in the initial treatment phase did not predict ADHD symptoms at follow-up, nor did the use of medications at each of the follow-up time points. Seventy-nine percent of those who had ADHD at Year 6 were on medication. Strikingly, the same proportion of children who did not meet criteria for ADHD also remained on a medication.

Some limitations of the PATS warrant attention. The PATS examined the effects of immediate-release MPH due to regulatory constraints and relatively limited availability of extended-release formulations at that time and maximum daily doses were limited to 30 mg per day. Clinical experience highlights the challenges of three times per day dosing, making use of extended-release MPH an appropriate intervention if a patient tolerates the equivalent dose of immediate-release MPH (Gleason et al., 2007). Additionally, generalizability to more diverse socioeconomic groups may be limited (Riddle et al., 2013).

Amphetamine formulation (D-amphetamine or mixed amphetamine salts [MAS]) are second-line treatment for preschool ADHD due to less empirical support (Gleason et al., 2007). Despite the historical FDA indication, no large-scale randomized clinical trials examine the efficacy of MAS in preschoolers. One prospective open trial of 28 preschoolers (ages 4 years to 5 years, 9 months) demonstrated safety and efficacy of MAS and stimulants with clinically significant changes in behavior ratings (Short, Manos, Findling, & Schubel, 2004). In older children, amphetamines are recommended as an appropriate first-line medication for ADHD, because they are equivalent to MPH for treating ADHD (Pliszka, 2007). As such, with the understanding that amphetamines are approximately twice as potent as MPH, appropriate dosing of amphetamines may be inferred from the PATS data.

Two other classes of medication, atomoxetine and alpha-agonists, are considered third-line ADHD treatment for preschoolers (Gleason et al., 2007).

In an 8-week, double-blind, placebo-controlled randomized clinical trial of atomoxetine in 101 5- and 6-year-old children, Kratochvil et al. (2011) compared atomoxetine and placebo in treating ADHD symptoms. Atomoxetine was titrated from 0.5 mg/kg to a maximum dose of 1.8 mg/kg per day on the basis of patient response, tolerability, and clinical judgment. Compared to placebo, atomoxetine was associated with improvement on the parent-reported ADHD Rating Scale (ADHD-RS), but less response on the clinician-rated ADHD-RS. Only 40% of atomoxetine-treated subjects were rated as *much* or *very much improved* at the conclusion of the study, and clinically significant symptoms remained for the majority of the children treated with atomoxetine. Though generally well tolerated, subjects who received atomoxetine were significantly more likely to experience decreased appetite, gastrointestinal upset, and sedation. Mood lability and irritability were also observed, with mood lability experienced in 41% of study participants versus 21% in the placebo group (Kratochvil et al., 2011).

Alpha-agonists are commonly used to treat preschoolers with ADHD (Rappley et al., 1999; Zito et al., 2000, 2007). The data supporting the use of alpha-agonists to treat ADHD in preschoolers includes open trials and retrospective chart reviews that include children as young as 4 years old (Hunt, Arnsten, & Asbell, 1995; Prince, Wilens, Biederman, Spencer, & Wozniak, 1996). In older children, alpha-agonists have smaller effect sizes than stimulants, but they are more effective than placebo (Scahill, 2009). Fatigue is the most commonly reported adverse effects in preschoolers (Lee et al., 2015). Because of the potential for death with overdose, these medications require education of parents regarding the importance of safe administration and storage (Lovegrove et al., 2014).

Disruptive Behavior Disorders

Disruptive behavior problems are among the most common disorders for which young children are brought for mental health care and among the best-studied disorders in preschool interventions. Hundreds of randomized trials demonstrate the efficacy of parent management training models in reducing symptoms of disruptive behaviors in young children (as reviewed in (Eyberg, Nelson, & Boggs, 2008). Currently, there are no randomized controlled trials of psychopharmacological interventions specifically targeting oppositional defiant disorder (ODD) or conduct disorder (CD) in preschoolers, and most reports focus on specific symptoms of disruptive behavior disorders, such as aggression. As a secondary outcome in a randomized controlled trial of MPH for 31 preschoolers with ADHD, parents reported significantly greater improvement in behavior of children on MPH, although differences in observed compliance were not reported (Firestone, Musten, Pisterman, Mercer, & Bennett, 1998). The largest of the reports was a retrospective chart review of 20 children under age 6 with aggression related to ADHD, post-traumatic stress disorder (PTSD), as well as ODD, who were treated with a number of different medications or combinations of medications (Staller,

2007). A small retrospective review of eight children ages 4–7 treated with risperidone suggested promising findings of reduced aggressive behaviors associated with various diagnoses (Cesena, Gonzalez-Heydrich, Szigethy, Kohlenberg, & DeMaso, 2002). A prospective open-label study of 12 developmentally typical preschoolers with comorbid ADHD and CD, resistant to prior treatment trials, who were treated with risperidone, is also available. Of the 12, eight children completed the 8-week follow-up, with significant and substantial decrease in the severity of signs of CD and ADHD (Ercan, Basay, Basay, Durak, & Ozbaran, 2011). Side effects of the risperidone at doses from 0.25 to 1.5 mg per day were limited, with the exception of an asymptomatic increase in prolactin to over fivefold normal levels.

This limited evidence base supporting psychopharmacological interventions for disruptive behaviors in preschoolers is striking given the significant impairment associated with these disorders and the often limited access to the well-studied psychotherapeutic interventions. Psychopharmacological treatment recommendations must be made in the virtual absence of rigorous data to support them and must therefore be extrapolated from data related to comorbid conditions or data in older children.

When medications are considered for children with disruptive behavior disorders, treatment of comorbid ADHD is a first-line intervention because of the higher level of empirical data to support stimulant use in preschoolers compared to other medications (Gleason et al., 2007). In older children, stimulants, atypical antipsychotic agents (especially risperidone), and lithium have been shown to be effective in addressing pediatric aggression in meta analyses (Knapp, Chait, Pappadopulos, Crystal, & Jensen, 2012). Extrapolating to young children, stimulants remain a first-line treatment because of safety profiles. Risperidone, with its FDA indication in children as young as age 5 (with autism) and relatively more safety data than other atypical antipsychotic agents, can be considered the second-line pharmacotherapy approach (Cesena et al., 2002; Masi, Cosenza, Mucci, & Brovedani, 2003; Mukaddes, Abali, & Gurkan, 2004). Dosing is informed by published reports of risperidone in preschoolers with a range of disorders, with reported doses of 0.125 mg per day up to 1.5–2.0 mg/day (Biederman et al., 2005; Cesena et al., 2002; Ercan et al., 2011; Luby et al., 2006). Weight gain (up to 5 kg in 6 months) and transient sedation have been associated with risperidone treatment in young children (Biederman et al., 2005; Luby et al., 2006; Masi et al., 2003). Titration and monitoring of atypical antipsychotic agents in preschoolers should generally follow the AACAP practice parameter on atypical antipsychotic agents (Findling, Drury, Jensen, & Rapoport, 2011). The one exception is routine prolactin monitoring. To date, every published report that has measured prolactin in preschoolers who were prescribed an atypical antipsychotic agent has described increases of at least 300%. Given the lack of developmental information about this substantial elevation in this age group, it seems prudent to discuss this possibility during the informed consent process and to track levels during treatment in preschoolers. Risperidone should be discontinued after 6 months to reassess underlying symptoms. The existing level of evidence

does not provide clear guidance regarding a second-line medication for severe disruptive behavior disorders in preschoolers, although other atypical antipsychotic agents, mood stabilizers, or stimulants have been used in older children (Farmer, Compton, Burns, & Robertson, 2002; Pappadopulos et al., 2003; Spencer et al., 2006; Steiner, Saxena, & Chang, 2003).

Major Depressive Disorder

Major depressive disorder is among the best studied disorders in preschool mental health (see Luby & Belden, Chapter 7, this volume). In contrast, research examining treatments for depression lags behind other disorders. Only one rigorous study has examined the effects of enhanced parent–child interaction therapy–emotion development (PCIT-ED) for preschool depression (Luby, Lenze, & Tillman, 2012). Although the study was small, promising outcomes included improved ability to recognize emotions and executive function–emotional control. Additionally, parent depressive symptoms declined in the treatment group but not in the psychoeducation group. There was no difference between groups in declines in depression scores for the PCIT-ED group compared to a parent education group. The finding that both the active treatment and psychoeducation resulted in significant decreases in depression supports anecdotal clinic experience that depressive symptoms in preschoolers tend to respond even to nonspecific therapy. Interestingly, we are not aware of any reports describing the efficacy of medication in treating preschool depression. One review of the adverse effects of SSRIs in anxious and depressed children under age 7 reported behavioral activation in more than one out of five children, and about that number discontinued treatment due to adverse effects (Zuckerman et al., 2007). Based on the lack of evidence, psychopharmacological treatment is not considered first-line treatment for preschoolers with depression. SSRIs are the empirically supported medications for older children with depression. For this reason, they are the medications of choice in the very rare cases when children have severe and impairing symptoms that are resistant to all available therapeutic interventions, including environmental approaches such as treatment of parental depression.

Other Mood Disorders

Bipolar disorder remains a controversial area in the world of preschool psychopathology. In the only epidemiologic study that included a bipolar disorder module, none of the 1,250 Norwegian preschoolers in the study met criteria for bipolar I disorder (Wichstrøm et al., 2012). In a study of 303 U.S. preschoolers with mood problems, a structured psychiatric interview identified 26 preschool children who met the criteria for bipolar I and showed some stability over time (Luby & Belden, 2006). Despite this valuable contribution, the field has not reached consensus regarding the validity of the diagnosis in preschoolers. Less controversial but similarly unresolved, a reanalysis of

epidemiological data demonstrated a rate of 3.3% of preschoolers who met all but the age criteria for dysregulated mood disorder with dysphoria (DMDD), with moderate rates of comorbidity with ADHD, ODD, and depressive disorders (Copeland, Angold, Costello, & Egger, 2013). The DSM-5 criteria for DMDD explicitly exclude preschoolers. Interestingly, many more publications focus on treatment of presumed bipolar disorder in preschoolers than on the validity of the diagnosis. PCIT, modified to address emotional dysregulation, may be promising (Luby, 2013).

In the only controlled psychopharmacological trial, risperidone and valproate were compared to placebo in preschoolers diagnosed with bipolar disorder. In 46 children with a clinical diagnosis of bipolar disorder, preschoolers on risperidone showed a significant decrease in the Young Mania Rating Scale (YMRS) compared to children on valproate or placebo (Kowatch et al., 2015). However, children on risperidone also showed a significant weight gain (0.7 kg in 6 weeks) and increase in prolactin (from 8 to 53 nanograms/ml), as well as other metabolic effects. The authors urge caution given these adverse effects. A number of other medications, including mood stabilizers, atypical antipsychotic agents (sometimes in combination with stimulants), alpha-agonists, and typical antipsychotics have been described in less rigorous methodologies, which limits the interpretability and generalizability (e.g., Biederman et al., 2005; Joshi et al., 2012; Pavuluri, Janicak, & Carbray, 2002). Although the controversy regarding the lack of compelling data supporting the validity of this diagnosis in preschoolers continues, there is no doubt that preschoolers can present with severe mood, sleep, and dysregulation patterns, which may be chronic or episodic. Treatment of the comorbid conditions with empirically supported interventions must be the first-line intervention, and treatments that address the emotional dysregulation using dyadic or family approaches have face validity. Caution with regard to medications that may cause metabolic and endocrine derangements is warranted. Further examination of complex mood disorders in preschoolers, with attention to distinguishing among clinical syndromes suggestive of depression, DMDD, and bipolar, will be necessary for the field to progress toward children receiving the safest, most effective treatment.

Anxiety Disorders

Anxiety disorders, including separation anxiety disorder, generalized anxiety disorder, selective mutism, and specific phobia, have been studied as a group in some preschool literature. The existing treatment data suggest that a 6- to 12-week psychotherapy trial may be effective in reducing signs of anxiety in preschoolers, using models based on cognitive-behavioral therapy (CBT) and PCIT (e.g., Comer et al., 2012; Donovan & March, 2014). An informal survey of participants at a national presentation on preschool psychopharmacology found that respondents' practice patterns were consistent with most respondents treating anxious preschoolers psychotherapeutically for at least 3 months before considering medication treatment (Gleason, 2007).

Data related to psychopharmacological treatment of anxiety disorders in preschoolers are scant. There are no randomized controlled studies of psychopharmacological interventions in preschoolers with anxiety disorders. Most reports on psychopharmacological anxiolytic agents in preschoolers focus on premedication for medical and dental procedures or toxic ingestions of benzodiazepines (e.g., Wiley & Wiley, 1998). There are a handful of case reports representing the published preschool anxiety disorder literature, excluding PYSD and OCD (Avci, Diler, & Tamam, 1988; Hanna, Feibusch, & Albright, 2005; Wright, Cuccaro, Leonhardt, Kendall, & Anderson, 1995). In these individual case reports, fluoxetine and buspirone are described as part of the effective treatment approaches for selective mutism and other disorders. The single-case methodology does not allow generalized conclusions.

In randomized controlled trials in older children, published reports demonstrate the superiority of fluoxetine, sertraline, venlafaxine, duloxetine, and fluvoxamine over placebo in treating children with anxiety disorders, with a mean overall effect size of 0.62 (Strawn, Welge, Wehry, Keeshin, & Rynn, 2014). The largest effect sizes were reported for sertraline and fluvoxamine. Notably, in the landmark Child Anxiety Medication Study, combination treatment was superior to either CBT or sertraline alone in acute treatment and at follow-up, highlighting the importance of therapy in anxiety disorders (Walkup et al., 2008). Extrapolating from the limited evidence available, fluoxetine, sertraline, or citalopram may be considered the first-line treatment for preschool anxiety resistant to adequate trials of age-appropriate psychotherapy. Fluoxetine has been used most extensively in children and adolescents, and has the strongest safety profile, at least in studies of depression (Whittington et al., 2004), and sertraline and citalopram have similar use histories in children. All three of these medications are available as liquids, although the alcohol-based sertraline may not be palatable to preschoolers.

In the absence of guiding principles for treatment decisions, parent preference and family history of response may also influence choice of medication, should it be considered. Starting doses as low as 5 to 8 mg of fluoxetine may be appropriate, with one-fourth of the lowest dose of other medications as reasonable starting doses for preschoolers. With the preponderance of evidence supporting psychotherapeutic interventions, a failed SSRI trial warrants careful reassessment and reconsideration of the diagnosis prior to a second SSRI trial. It should be noted that benzodiazepines, tricyclic antidepressants, and busipirone have not been rigorously studied in preschoolers, and are associated with potential risks, including overdose by ingestions of benzodiazepines and tricyclic antidepressants.

Posttraumatic Stress Disorder

PTSD is among the best-studied preschool anxiety disorders in terms of the diagnostic criteria and treatment approaches. In DSM-5, the first developmentally specific diagnostic criteria were included for preschool PTSD. Two

well-supported treatment modalities, child–parent psychotherapy (CPP) and preschool CBT, have demonstrated sustained decreases in symptoms and diagnosis in preschoolers with PTSD (Cohen & Mannarino, 1996, 1997; Lieberman, Ippen, & Van Horn, 2006; Lieberman, Van Horn, & Ippen, 2005). Both may be considered first-line treatments for PTSD. Play therapy, though not supported by randomized controlled trials, has been used extensively in treating trauma-exposed preschoolers (Gaensbauer, 2000, 2002).

No studies in preschoolers and only two randomized controlled trials have examined psychopharmacological interventions for PTSD in children. Compared to CBT and to placebo, sertraline has shown no effect in treating pediatric PTSD (Cohen, Mannarino, Perel, & Staron, 2007; Wagner et al., 2004). Positive open-label trials for citalopram, extended-release guanfacine, clonidine, and risperidone are promising, although only clonidine and risperidone have been described in preschoolers (n = 7, n = 3, respectively; Connor, Grasso, Slivinsky, Pearson, & Banga, 2013; Harmon & Riggs, 1999; Meighen, Hines, & Lagges, 2007).

The lack of empirical data to guide pharmacologic treatment in a vulnerable population that experiences debilitating symptoms across a wide range of domains is striking. To extrapolate from promising but not rigorous trials in school-age children and adolescents to preschoolers with PTSD is a significant leap, and one that includes many unfounded assumptions. Every effort should be made to access quality therapy for preschoolers with PTSD, because these symptoms do not remit spontaneously (Scheeringa, Weems, Cohen, Amaya-Jackson, & Guthrie, 2011). If CBT is not available or is unsuccessful, treatment of comorbid conditions with therapy and, if appropriate, pharmacologically, should precede attempts to treat PTSD with medications. Targeted approaches, such as addressing sleep problems, may be considered before extrapolating further. Because of the support for alpha-agonists, albeit admittedly weak, in both preschoolers and older children, experience in safety for preschoolers with cardiac anomalies, and the compelling theoretical rationale for targeting the autonomic nervous system in children with PTSD, this class of medication may be considered after failure of multiple psychotherapeutic approaches.

Obsessive–Compulsive Disorder

Signs of obsessive–compulsive disorder (OCD) have been described in young children, although studies establishing the validity of the categorical disorder have not been published. It is considered separately because the treatment approaches in older children require somewhat different treatment than other anxiety disorders, and the underlying pathophysiology is thought to differ as well. OCD is thought to be rare in the preschool population, with a rate of 0.3% reported in one study, while rates in school-age children are reported to be 3% (Coskun & Zoroglu, 2009; Wichstrøm et al., 2012). Although treatment recommendations in 2007 proposed CBT as first-line treatment

for preschool OCD (without data from preschool subjects), rigorous trials have been published more recently, supporting the recommendation, with decreased symptoms of OCD after family-focused exposure plus response prevention treatment (Lewin et al., 2014). Descriptions of psychopharmacology interventions include use of sertraline and fluoxetine in Turkish children ages 30 months to 5 years. In three reports, severe behavioral disinhibition developed in nine of the 13 children. Of these, three responded to lowering the dose of SSRI and three received atypical antipsychotic agents. The rates of disinhibition in these few case reports are higher than those in the larger chart review by Zuckerman et al. (2007). These differences may be related to dosing, titration schedules, something specific to children with OCD, or other factors in these selected cases. It is impossible to generalize from these reports, but caution is clearly warranted when considering medications in preschoolers with OCD, which should be considered only after failure of CBT and with extreme impairment.

Autism Spectrum Disorder

Approximately 10% of preschoolers ages 2–5 with an autism spectrum disorder (ASD) take a psychotropic medication, most commonly stimulants and antipsychotic agents (Mire, Raff, Brewton, & Goin-Kochel, 2015). As a neurodevelopmental disorder with impairment across multiple domains and often comorbid with other psychiatric disorders, a range of interventions is generally needed, including speech–language therapy and occupational therapy, as well as applied behavioral analysis to target the core symptoms. Factors, including variable verbal abilities, representational capacity, and motivation for social engagement have the potential to limit the adaptation of empirically supported psychotherapies to children with ASD. This may in part explain the higher rates of psychotropic medications being prescribed for preschoolers with ASD. Efforts to adapt empirically supported treatment originally designed for other preschool psychiatric disorders for children with ASD are being developed, although large rigorous studies have not been done. For example, adaptations of PCIT have been described for children with ASD and comorbid disruptive behavior problems, and CBT was effective in a child with ASD and anxiety (Lesack, Bearss, Celano, & Sharp, 2014). Psychopharmacological intervention to address the core symptoms of autism has had mixed results in preschoolers. Two randomized controlled trials of risperidone focused on preschoolers specifically. One study of 24 preschoolers reported modest improvement in core symptoms on the Child Autism Rating Scale compared with placebo over 6-month period (Luby et al., 2006). The other study of 39 children ages 2–9 years (mean age 60 months) reported a more robust effect of risperidone on core symptoms compared to placebo (Nagaraj, Singhi, & Malhi, 2006). Studies in older children have included children as young as 4, but such wide age ranges make it difficult to apply these findings directly to preschoolers (Aman et al., 2009; McDougle et al., 2005). In the one study that focused on

preschoolers with signs of ADHD and ASD, 50% of children responded to MPH, with at least 30% improvement on approximately 15 mg/day divided into two doses (Ghuman et al., 2009).

In preschoolers with ASD, it is most important that children receive applied behavior analysis (ABA) or other ASD-specific behavioral approaches as well as speech and occupational therapies for treatment of the core symptoms. The effect sizes noted in the two randomized controlled psychopharmacological trials for core symptoms of ASD are substantially lower than the effect size of the well-supported ABA intervention. Given the potential adverse effects of risperidone, it should only be considered as a treatment for core symptoms if they are extreme and other services are not available. Psychopharmacological treatment focused on comorbid disorders that do not respond to modified psychotherapeutic approaches may be considered. Generally, in children with neurodevelopmental disorders, starting with lower doses than those prescribed for typically developing children is recommended given the potential for adverse effects.

PUBLIC POLICY

In the last decade, a number of states have implemented approaches intended to increase children's access to appropriate treatments and to reduce inappropriate exposure to psychopharmacological agents. Much of the policy has focused on the use of atypical antipsychotic agents, although the focus has not been solely on the preschool population. In fact, in 2014, the Health Care Effectiveness Data and Information Set (HEDIS) added three measures that focus on use of antipsychotic agents. States must report (1) rates of children on concomitant antipsychotic agents, (2) percentage of children on antipsychotic agents receiving metabolic monitoring, and (3) rates of psychosocial treatments in children on antipsychotic agents. (*www.ncqa.org/portals/0/homepage/antipsychotics.pdf*). These reporting requirements will increase all states' attention to pediatric prescribing and yield valuable information about practices related to preschoolers.

States have developed specific models of intervention. In Louisiana, the Medicaid managed care organization has supported training in early childhood-focused psychotherapies for Medicaid mental health providers, resulting in an increase in the workforce able to address the needs of young children with effective treatment, although access continues to be limited, especially in rural areas. In Maryland, antipsychotic prescriptions for young Medicaid-insured children require a preauthorization form that is reviewed by a clinical pharmacologist within 1 day, with the potential for review by a child and adolescent psychiatrist. Preauthorization requires demographic information, psychosocial treatment, laboratory results, and growth parameters. If approved, the case is reviewed in 90 days, with attention to treatment outcome and appropriate monitoring. In Washington, mandated reviews are triggered

by specific criteria, such as age or indication, and the state Medicaid system offers voluntary phone consultation as well (Hilt et al., 2010). This program resulted in a 38% decrease in antipsychotic prescriptions for children under age 5 between 2007 and 2010. North Carolina developed A+ Kids, a registry for children on antipsychotic agents, in which providers complete demographic information, laboratory data, growth parameters, and diagnosis when they prescribe an antipsychotic agent for a child under 12 who is covered by Medicaid (Christian et al., 2013). Registration in North Carolina does not involve prior authorization or regulations about which medications may be used. Preliminary data suggest a decline in prescriptions within 1 year of implementing the registry. A caveat comes from a study of a Mid-Atlantic state that implemented prior authorizations for antipsychotic prescriptions: While demonstrating a reduction in prescriptions for older children, they found no effect in children ages 0–5 compared to prescription rates in a state that made no policy changes (Stein et al., 2014). A number of explanations for this finding are possible, but it highlights the need for policy not only to create "speed bumps" for higher-risk treatment approaches but also to ensure access to safer alternatives.

CONCLUSIONS

In the last decade, the profile of medications young children are receiving has changed; although the overall rate of prescriptions has not increased, it continues to outpace the evidence. Awareness of the knowledge gaps seems to be increasing with growing attention to the need for access to quality care. However, in much of the country, providers and families find themselves in the position of making decisions that cannot be guided by evidence and that often involve choosing what is available rather than what is indicated. Clinicians sometimes find evidence-informed recommendations unrelated to their practice reality, in which there is limited access to the quality psychosocial interventions that serve as better studied, more effective, safer alternatives to psychopharmacological interventions. However, acknowledging the major gaps in our knowledge and/or our local resources is necessary to provide fully informed consent to families and to advocate locally and more broadly for access. When the highest quality evidence-based treatment is not available, principles or components of the effective treatment may be offered (Wissow et al., 2008). While such an approach is not yet supported by rigorous evidence, a growing movement is examining the active components of evidence-based treatments (Kaminski, Valle, Filene, & Boyle, 2008). Judicious prescribing, based on careful assessment and formulation, matching treatment to the diagnosis, and tracking treatment effects systematically are important steps that cannot be overlooked. Although apparently less effective in preschoolers than in older children, psychopharmacological treatment may be a valuable component of a treatment plan for a very young child with severe psychopathology.

Currently, most treatment plans are made without true options, due to

limited access to treatments and/or lack of safety and efficacy information about medications. To serve children adequately, a number of steps are needed at community and policy levels. First, children need greater dissemination of effective psychotherapies. Although they are not panaceas, these interventions have substantial empirical support that suggests widespread access could have significant effects on young children's development. Second, disorders that are not fully characterized in preschoolers must be rigorously validated. It is imperative that clinicians know what they are treating in order to guide treatment decisions. Third, research to examine safety and efficacy of psychopharmacological agents is necessary to allow truly informed consent discussions. Rigorous evaluation of innovations at state and local levels will offer dissemination of the most promising approaches to serving young children.

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16

Integrating Translational Developmental Neuroscience into Early Intervention Development for Preschool Psychopathology

A Proposed Model and Example

Michael Gaffrey

Because of the recognition that current treatments for pediatric psychiatric conditions have modest effect sizes overall (Tsapakis, Soldani, Tondo, & Baldessarini, 2008; Weisz, McCarty, & Valeri, 2006), enthusiasm for intervention development that translates well-characterized neurobehavioral mechanisms into novel treatments has been rapidly growing (Insel & Gogtay, 2014). The intuitive appeal of this approach, previously referred to as translational developmental neuroscience (TDN) by the National Institute of Mental Health (NIMH; 2008; Bar-Haim & Pine, 2013), lies in bridging experimental research on basic affective or cognitive mechanisms (and associated neural substrates) with the study of individual differences in these mechanisms and their relationship to early emerging psychopathology. By leveraging findings from basic research, including well-developed models of mechanism and neuroanatomy, TDN suggests it is possible to generate hypotheses about specific functional treatment targets and develop interventions intended to engage and alter them in child populations. Importantly, given an increasing consensus

that many psychiatric conditions have their roots in early development (Bale et al., 2010; Insel, 2014), TDN-informed interventions may also offer more permanent and lasting benefits for interventions occurring very early in life (e.g., early childhood) given the greater neural plasticity during this period (Fox, Levitt, & Nelson, 2010).

However, despite growing enthusiasm for neuroscience-informed approaches to early intervention, very few attempts have been made to articulate specifically how neuroscience can be used to more fully inform treatment development. This is not to say that well-known principles such as neuroplasticity have not been integrated into developmental models of psychopathology, because they have. Nor is it to say that treatment development efforts targeting preschool psychopathology have not integrated neuroscience principles of brain plasticity into their theories of therapeutic change. Rather, what I suggest here is that this previous work generally has neither discussed nor fully considered how current theories of normative brain development processes can be incorporated as a foundational element guiding the development of very early interventions. To be sure, this is no small feat, and our continually evolving understanding of how the brain develops will most certainly preclude any definitive answer at this time, or any time in the near future. Nevertheless, recent neurobiological reviews of brain development and psychopathology suggest that the field is now at a tipping point for identifying advantageous paths forward in this developing area of study (Bar-Haim & Pine, 2013; Hulvershorn, Cullen, & Anand, 2011; Monk, 2008).

My goal in this chapter is to suggest one path forward for translating well-characterized neurobehavioral mechanisms into novel treatments for preschool psychopathology. Specifically, I suggest that by integrating normative theories of functional brain development into well-developed models of development and psychiatric phenotypes, it is possible to identify key neurobiological treatment targets and inform how early intervention strategies might be able to engage and positively alter them. In recognition of the important roles of developmental stage and environmental context, I first discuss how this integration is best accomplished through the use of a developmental psychopathology framework. Building on this, I then suggest a treatment development pathway, beginning with the initial identification of neurobiological mechanisms to be targeted during intervention and ending with the eventual dissemination and implementation of the given treatment. In order to provide an illustrative example of how this treatment pathway might be applied, I use negative attentional bias and its relationship with disrupted information processing in depression as an exemplar. I conclude the chapter by suggesting future directions that may help address some of the outstanding gaps in our knowledge about early emerging psychopathology and its interaction with normative brain development processes, information that is considered critical for future TDN treatment development efforts targeting preschool psychopathology.

DEVELOPMENTAL PSYCHOPATHOLOGY: A THEORETICAL ANCHOR FOR INTERVENTIONS TARGETING PRESCHOOL PSYCHOPATHOLOGY

Although rapid advances in technology have offered new and exciting opportunities to examine preschool psychopathology in unprecedented ways, their continued use in the absence of a developmentally informed conceptual framework is unlikely to move our understanding of psychopathological brain processes beyond the "what" and "where" of differences to the more central questions of "when" and "how" they arose (Cicchetti, 1984). The adoption of such a conceptual framework is uniquely important for understanding how early interventions can most effectively capitalize on normative developmental phenomena, which, by their very nature, are perhaps best captured by an examination of process rather than outcome. I believe that such a framework should have several features in order to be useful for this purpose. Succinctly, such a framework must sufficiently capture the complex nature of factors affecting disorder onset and course, as well as define development as an ongoing process. Furthermore, the given framework must be broad enough to consider the interplay between multiple relevant factors (e.g., psychological, biological, environment), allow for the incorporation of other complementary theories related to more specific processes of interest not fully captured within it (in our case, brain development), and explicitly define development as a process that has no hard-and-fast end point (i.e., does not end at a specific age or milestone). Perhaps most importantly, and following previous discussions of bioecological theories of development and resilience (Ungar, Ghazinour, & Richter, 2013), it must provide guidance for defining optimal treatment target(s) and response(s) based on their functional utility within a given environment, that is, recognizing that definitions of behavior and associated brain function as "functional" versus "dysfunctional" are contextually bound and not the characteristic of any single level of the complex systems (e.g., "in" the individual) within which children live. The previously articulated developmental psychopathology perspective (Cicchetti & Toth, 1998; Cicchetti, 1984; Sroufe & Rutter, 1984) offers a powerful framework that includes each of these elements and comes with a well-established history of being applied to early emerging psychopathology and treatment development (Cicchetti & Toth, 1998). I believe that adopting this general framework provides an important theoretical grounding for a systematic and developmentally sensitive TDN approach to intervention development for preschool psychopathology.

THE BRAIN AS A COMPLEX SELF-ORGANIZING SYSTEM

Harnessing brain plasticity mechanisms for therapeutic interventions is not new (for a comprehensive review, see Cramer et al., 2011), and for some time it has been used regularly to develop rehabilitation programs targeting the

behavioral sequelae of neurological conditions such as stroke or traumatic brain injury. Although this work has provided foundational guidance for how neuroscience can be used to inform treatment development, our rapidly growing understanding of brain development as a self-organizing process suggests that these models are unlikely to be suitable for informing how neuroscience can guide the development of early preventive interventions (Cicchetti & Curtis, 2006). In other words, understanding the active role of the individual in determining what experiences influence the process of brain development is likely to prove critical for developing effective preventive interventions for preschool psychopathology. More specifically, given the growing consensus that most psychiatric disorders are neurodevelopmental in nature, physiological and psychological experiences of early illness expression are highly likely to drive key neural systems in the direction of ever-more dysfunctional configurations and further perpetuate illness-related behaviors over time. As a result, the expression and course of psychopathology are likely to be heavily influenced by individually encountered physical and social environments, including social–emotional learning and attachments, interpersonal experiences, psychological trauma, internal representations of self and others, and social–cultural influences (Grossman et al., 2003). As a result, interventions seeking to positively alter the early emerging disruptions in brain development associated with psychopathology must also attend to the various ways that social–emotional contexts can influence motivation, treatment adherence, and treatment response over the course of development (Meltzoff, Kuhl, Movellan, & Sejnowski, 2009). As detailed below, I believe that integrating a self-organizing view of brain development with recent theoretical work on the developmental emergence of brain function will be highly useful for generating novel treatment targets and approaches for early emerging psychopathology.

THE DEVELOPMENT OF SPECIALIZED BRAIN FUNCTION

While a self-organizing view provides a powerful theoretical context for conceptualizing how individual experience may affect connections and/or activity within the developing brain, it remains agnostic as to how brain regions and/or cortical circuits associated with a specific behavior or cognition emerge and form specific connections over the course of development. Interactive Specialization (IS), a recently proposed conceptual framework of normative brain development (Johnson, 2000, 2001, 2011), suggests that brain regions begin to take on increasingly specific functional roles (i.e., functional specialization) as activity-dependent interactions with other regions shape and eventually restrict their sensitivity to specific sets of stimuli (e.g., faces or events). Thus, similar to the use-dependent properties of neurons described in studies of neural plasticity (Huttenlocher, 2002), IS suggests that brain regions and related networks are progressively "fine-tuned" (i.e., constrained) into a mature form following repeated exposure and involvement with a given task

and/or environment (Johnson, 2001). IS also suggests that the development of a new skill or the onset of an experiential event (e.g., adolescence) may alter previously established interactions between brain regions and lead to large-scale reorganization of brain function as a result. Thus, IS emphasizes the importance of interregional connectivity between brain regions for emerging functional specialization, as well as the possibility of later occurring experience-dependent reorganization across development.

The IS framework has previously been compared to other general theories of brain development, including maturational and skill-learning viewpoints (Johnson, 2001). Briefly, the maturational viewpoint of brain development suggests that new skills or behaviors are associated with the anatomical maturation of a specific brain region. Underlying this relationship is an assumption that neuroanatomical development can be used to identify the specific age at which a brain region will become fully "functional." As such, in the maturational model, the specialized function of a brain region emerges over time in a linear and deterministic fashion and is static once established, ruling out periods of dynamic reorganization of brain function and associated networks across development. Alternatively, skill-learning views of brain development suggest that brain regions used for complex skill acquisition in adults are highly similar to those necessary for the emergence of new skills earlier in development. Thus, while the exact form of the skill to be acquired at a given developmental period may differ, the pattern of brain activity necessary to support it may not.

In general, while the theories discussed earlier are not necessarily mutually exclusive, the IS framework is unique when compared to the maturational and skill-earning perspectives given its specific predictions about developing functional specialization within the brain, and the underlying assumption that skill development is dependent on the interregional interactions of cortical areas rather than fully preprogrammed maturational processes or patterns of skill acquisition. Importantly, it also recognizes that brain development is a transactional process, in which genes, behavior, and environment each play an important role in the developmental of functional specialization (Johnson, 2011). These distinctions are important given a growing body literature suggesting that functional brain development is a prolonged process with changing patterns of within- and between-network connectivity (Dosenbach et al., 2010) open to environmental influence (Bluhm et al., 2009; Emerson & Cantlon, 2012; Thomason et al., 2008; Thomason, Yoo, Glover, & Gotlib, 2009).

DEVELOPING BRAIN FUNCTION AND EARLY INTERVENTION DEVELOPMENT

As a domain-general framework for brain development (Johnson, 2011), IS does not provide explicit predictions about the potential effects of specific

individual differences and developmental histories on developing brain networks. Rather, it hypothesizes a developmental process and provides a general set of testable predictions that can be used to explore the development of previously proposed networks associated with a construct (e.g., emotion regulation) and the potential influence of environmental events, such as early intervention, on them (see Table 16.1). In line with the view that the development of brain function is an emergent process, IS also predicts that the influence of experience on this process will vary as a function of developmental timing, with early experiences likely resulting in more variable consequences for ongoing brain function and organization when compared to those occurring after networks are likely already firmly established (i.e., in adulthood; (Johnson, 2011).

Research investigating brain development and its relationship with increasingly complex behavior continues to provide highly novel insights supporting IS predictions and the importance of this transactional process. This work has been perhaps most informative when focused on periods of rapid change in specific developmental abilities. Perhaps the most illustrative example comes from a large body of research investigating language development during infancy, in which infants have been shown to have the capacity to distinguish all sounds across multiple languages very early in development (Kuhl, 2000). As infants age, this capacity narrows, and by 1 year of age, infants' ability to perceive sound distinctions used only in foreign languages and not their native environment is significantly weakened (Kuhl et al., 2006). Importantly, increasing sensitivity to native phonemes (relative to non-native phonemes) during infancy has been found to be associated with parallel increases in neural sensitivity to these sounds that are predictive of later language learning. More specifically, infants with enhanced event-related potential (ERP) responses to native phonemes at 7.5 months show faster advancement in language acquisition between 14 and 30 months of age (Kuhl et al., 2008).

TABLE 16.1. Normative Patterns of Functional Brain Development Predicted by Interactive Specialization

1. Increasing specialization of a brain region will be evidenced by a more selective response patterns within that region
2. Increasing specialization of a brain region will be evidenced by increasing localization (i.e., shrinking of cortical tissue/number of regions active in response to a stimulus)
3. Regions similarly responsive to a given stimulus at an earlier developmental point may no longer continue to coactivate during tasks once different patterns of functional specialization emerge for each
4. Develop functional specialization for cognitive skills or behavior will be associated with widespread changes across multiple regions.
5. Individual regions will mutually influence the development of functional specialization in each other and facilitate the emergence of tightly integrated, specialized networks

Previously referred to as "neural commitment" (Meltzoff et al., 2009), this phenomenon is believed to reflect the formation of neural architecture and circuitry dedicated to the detection of phonetic and prosodic characteristics of the particular native language(s) to which the infant is exposed. Following an IS interpretation of developing functional specialization, it also suggests that when a "neural commitment" to a specific language is fully realized, it likely interferes with the acquisition of a new language (Iverson et al., 2003). Importantly, and supporting the importance of early social relationships for successful learning, experiments also show that the computations involved in language learning are "gated" by social processes. For example, in foreign language learning experiments, social interaction strongly influences an infant's statistical learning. Infants exposed to a foreign language at 9 months learn rapidly, but only when experiencing the new language during social exchanges with other humans (Kuhl, Tsao, & Liu, 2003).

This sophisticated line of infancy research provides a powerful illustration of how neuroscience can add to our mechanistic understanding of developmental processes and inform early interventions targeting them. In line with the predictions of IS, it also suggests that by identifying early brain–behavior relationships critical to the development of a given characteristic or skill, it may be possible to alter the neurodevelopmental trajectories and long-term behavioral outcomes associated with them. Following this line of reasoning, and as illustrated in Figure 16.1, I suggest that rapid periods of development for a given characteristic or skill can be systematically identified and used to signal a "sensitive period" when the brain–behavior relationships underlying them are particularly malleable to environmental input. Within the context of early intervention, capitalizing on the potential for greater neuroplasticity during these periods is likely to prove most optimal for positively altering neurodevelopmental trajectories at the individual level. Thus, by understanding the relationship between a given individual characteristic and its association with developing psychopathology, interventions targeting the neural correlates of this association can then be developed and tested. While our developmental understanding of brain–behavior relationships and their relationship to emerging psychopathology during the preschool period is in its infancy, recent progress has provided some initial insights into how this model of treatment development may be applied to early emerging depression. Following the steps in Figure 16.1, I now detail how emerging research has (1) identified the first 5 years of life as a rapid period of developmental change in negative affect, and that individual differences in developmental trajectories of negative affect during this period are predictive of later depression; (2) provided initial evidence supporting a link between negative affect (a key symptom of depression) and amygdala reactivity to emotional stimuli in preschool-age children; (3) established a critical role for negative attentional biases (NAB) in depression and indicate that NAB are already related to depression in preschoolers; and (4) suggested that attention bias modification

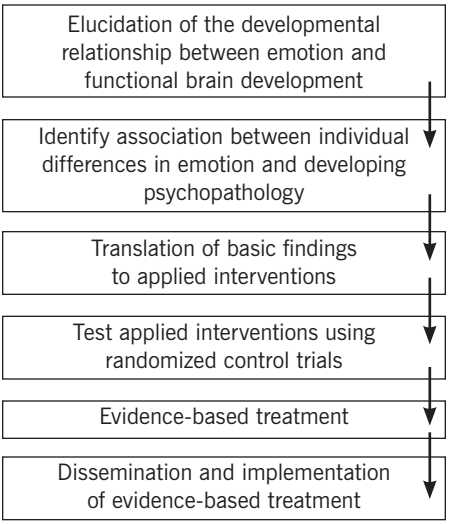

FIGURE 16.1. Proposed treatment development pathway illustrating the integration of translational developmental neuroscience into the initial development of interventions for early emerging psychopathology. The model can also be applied to other domains (e.g., cognition) as well.

procedures may positively alter NAB in depression and be easily applied to very early forms of this disorder.

PRESCHOOL DEPRESSION: AN AREA IN NEED OF EVIDENCE-BASED TREATMENT DEVELOPMENT

A large body of research now supports the validity, clinical significance, and long-term negative impact of mood disorders that occur during the preschool period. Data supporting the validity and significance of preschool mood disorders are highly similar to those reported for older groups, including symptom specificity (Luby et al., 2002), familial transmission (Luby, Belden, & Spitznagel, 2006), disrupted stress reactivity (J. L. Luby et al., 2003), impairment across multiple contexts (Luby, Belden, Pautsch, Si, & Spitznagel, 2009), gene × environment interactions (Bogdan, Agrawal, Gaffrey, Tillman, & Luby, 2014), continuity over time (Luby, Si, Belden, Tandon, & Spitznagel, 2009), and altered functional brain activity and organization in regions important for emotion regulation (Gaffrey, Barch, Singer, Shenoy, & Luby, 2013; Gaffrey et al., 2011). Evidence demonstrating that disrupted mood and related emotional behavior during the preschool period are robust risk factors for

later DSM-5 mood and anxiety disorders at school age has also been provided (Luby, Gaffrey, Tillman, April, & Belden, 2014). For example, a recent study of preschoolers with early-emerging depression reported that more than 50% of these children went on to qualify for a DSM-5 diagnosis of major depressive disorder (MDD) within ~6 years of their initial identification (Luby et al., 2014). Yet, despite a rapidly growing body of evidence convincingly demonstrating that significantly impaired mood during the preschool period is strongly associated with long-term negative outcomes, interventions specifically targeting these disruptions are still in their infancy (Luby, 2013). Thus, with epidemiological studies suggesting similar prevalence rates for preschool- and school-age MDD (~1–2%; Egger & Angold, 2006), evidence-based treatment development for very early occurring depression is clearly an underserved need that is likely to prove critical in reducing the growing public health burden of this disorder.

THE DEVELOPMENTAL TRAJECTORY OF NEGATIVE AFFECT DURING EARLY CHILDHOOD

Developmental studies of negative affect in early childhood have generally focused on a child's behavior in reaction to situations perceived as novel and/or challenging. While measurement approaches have varied (behavioral observation, parent report, etc.), changes in child behavior indicating a low threshold for distress, sadness, anger, or fear during these types of situations have typically been used to define and measure individual differences in negative affect (Else-Quest, Hyde, Goldsmith, & Van Hulle, 2006). Interestingly, whether using observational or parent report measures, longitudinal studies have indicated that negative affect peaks at approximately 3 years of age, then steadily declines across the preschool period (Olino et al., 2011; Partridge & Lerner, 2007). Researchers have also suggested that although a normative pattern of declining negative affect is evident across early childhood, important individual differences in negative affect and its pattern of change over time are also evident (Partridge & Lerner, 2007). More specifically, where a child falls relative to his or her peers is likely to remain consistent across childhood (Neppl et al., 2010). For example, a toddler with relatively higher negative affect than his or her peers is likely to develop into a preschooler with the same profile. Interestingly, recent findings also suggest that a small percentage of very young children may also go on to exhibit further increases in negative affect as they age, which suggests not only persistently elevated negative affect compared to peers but also a worsening of functioning over time (Wiggins, Mitchell, Stringaris, & Leibenluft, 2014). Taken together, these data indicate that the proclivity to experience negative affect measured even at a single time point early in development is likely to be related in important ways to both the current and future functioning of an individual child. They also suggest that early childhood may be a critical developmental period for understanding how

the early origins of individual trajectories of negative affect relate to future risk for psychopathology.

NEGATIVE AFFECT DURING EARLY CHILDHOOD AND RISK FOR DEPRESSION

Research examining the relationship between early negative affect and later internalizing psychopathology, such as anxiety and depression, has suggested that elevated negative affect during early childhood is an important marker of risk. For example, at the symptom level, infants rated as "fussy" and "difficult to soothe" by their parents are also more likely to have higher scores on maternal ratings of depression and anxiety at 5 years of age (Côté et al., 2009). Similarly, high negative affect scores during the infancy and preschool periods have been associated with elevated parental ratings of anxiety and depression symptoms during later school age and adolescence (Dougherty et al., 2011; Karevold, Roysamb, Ystrom, & Mathiesen, 2009). More recent data suggests a similar phenomenon when diagnostic outcomes are considered. Specifically, elevations in negative affect at 6 years of age have been found to significantly increase the odds of receiving a diagnosis of depression at age 18 years (Bould et al., 2014). Studies investigating early irritability (i.e., easy annoyance and touchiness characterized by anger and temper outbursts) have also suggested a strong link between elevations in negative affect and later psychopathology. Of particular relevance for identifying young children at increased risk for psychopathology, Dougherty et al. (2013) reported that irritability measured at 3 years of age was predictive of depression and oppositional defiant disorder (ODD) diagnoses 3 years later (i.e., 6 years of age), over and above baseline diagnostic status. Furthermore, using measures controlling for item overlap, the authors also found that irritability measured when children were 3 years old predicted increases in dimensional measures of depression, ODD, and functional impairment at 6 years of age.

EARLY EMERGING NEGATIVE AFFECT AND BRAIN FUNCTION IN PRESCHOOLERS

Longitudinal studies suggest that elevated negative affect early in life is critically related to both current and future manifestations of clinical psychopathology, including depression. Nevertheless, not until recently have the neurobiological markers of early negative affect and their predictive value been examined in preschoolers. As I detail below, emerging data are beginning to suggest that amygdala reactivity to emotionally salient information is significantly related to, and predictive of, negative affect in preschoolers. In line with IS, understanding the early neurobiological roots of negative affect may prove critical for identifying preschoolers at increased risk for depression, as

well as developing early interventions that directly target them and potentially prevent their deleterious effects on developing neural networks.

AMYGDALA FUNCTION IN PRESCHOOLERS

Developmental neuroimaging studies of emotion suggest that the amygdala plays a central role in the early evaluation of, and subsequent response(s) to, emotional stimuli (Gaffrey, Luby, & Barch, 2013). Similar to the early developmental trajectory of negative affect, neuroimaging data suggest that the amygdala undergoes an extended course of structural and functional change during the infancy and preschool periods. Though still an emerging area of research, amygdala volume has been reported to increase rapidly during the first 5 years of life, reaching the potential peak volume during the school-age period (Giedd et al., 1996; Gilmore et al., 2012; Uematsu et al., 2012). Investigations of amygdala function during early childhood have been limited given the strict movement requirements of functional magnetic resonance imaging (fMRI). However, with an increased understanding of how to train young children successfully for the imaging environment, emerging data are beginning to provide insight into amygdala function in preschool-age children and how the amygdala changes across development. Most of the studies to date have used images of human faces displaying specific emotions given the well-established relationship between amygdala activity and face processing. While amygdala reactivity to facial expressions of emotion has been consistently reported, findings regarding differential *levels* of amygdala response to specific face types and how this develops have been mixed. For example, Todd and colleagues (Todd, Evans, Morris, Lewis, & Taylor, 2011) examined amygdala response to happy and angry facial expressions of emotion in preschoolers, school-age children, and adults. Region-of-interest analyses focusing on the amygdala revealed a linear relationship between age and activity in response to happy and angry faces over scrambled images, suggesting a developing sensitivity of the amygdala to facial expressions with age. Interestingly, when examining fearful versus neutral faces, Gee and colleagues (2013) reported that amygdala activity was greatest during early childhood and consistently declined into adulthood. While the developmental trends differ in these two studies, potentially due to stimulus type and/or comparisons examined, each suggests the amygdala is responsive to facial expressions of emotion in early childhood and raises the possibility that active developmental changes in amygdala response are likely already unfolding in this period.

AMYGDALA FUNCTION AND NEGATIVE AFFECT IN PRESCHOOLERS

While amygdala reactivity to emotional stimuli in young children has now been demonstrated, few studies have examined its relationship with early

childhood psychopathology. Of particular interest is whether differences in amygdala activity can be detected in young children who display high levels of negative affect, or whether individual differences in negative affect more broadly are associated with alterations in amygdala activity. In a recent study of face processing in preschool-age children with and without a very early occurring form of depression, my colleagues and I reported an association between preschool depression and increased activity in the right amygdala (Gaffrey, Barch, et al., 2013). Interestingly, and similar to previous research in older depressed groups (Lau et al., 2009; Yang et al., 2010), elevated right amygdala activity was found to be present in response to all face types in depressed preschoolers, including sad, happy, fearful, and neutral. Matching the few dimensional studies of amygdala activity and depression severity in children and adolescents (Barch, Gaffrey, Botteron, Belden, & Luby, 2012; Henderson et al., 2014), our follow-up analyses revealed that heightened right amygdala activity while viewing facial expressions of emotion was also correlated with elevated parental reports of negative affect across all children, suggesting that amygdala activity is sensitive to individual differences in child negative affect in both healthy and depressed preschoolers. More recently, prospective work examining the relationship between amygdala activity during face viewing and negative affect 12 months later in a subset of these children indicated that elevated amygdala activity while viewing facial expressions of sadness predicted increased negative affect 1 year later, over and above negative affect reported at baseline (M.S. Gaffrey, Barch, & Luby, 2016). As a result, amygdala activity early in life is critically related to current and future manifestations of negative affect.

AMYGDALA FUNCTION AND NAB

Building on previous research suggesting that elevated negative affect early in life is a significant predictor of later depression (Bould et al., 2014; Dougherty et al., 2013; Karevold et al., 2009), the previously noted findings suggest that variations in amygdala activity may be one of the key mechanisms contributing to this relationship. In addition, while these findings do not directly inform whether amygdala activity can serve as a predictor of future *diagnostic* status, they do raise the intriguing possibility that functional activity within the amygdala may serve as a significant biomarker that can identify children with increased, or increasing, risk for later negative affect and potential mood difficulties, including depression. Perhaps most importantly, they provide an initial link between a key feature of early behavioral risk for depression and function within a brain region consistently implicated in neurobiological models of depression (Drevets, Price, & Furey, 2008). Paralleling normative studies that have consistently linked increased amygdala sensitivity to salient emotional content, neurobiological models of depression have generally implicated heightened amygdala responses to negative emotional content as reflecting an increased bias for this type of information. More specifically, cognitive

models of depression suggest that NAB play an important role in the development and maintenance of depression (Beck, 2008). Given this, and emerging data linking amygdala activity to NAB (Britton et al., 2015), NAB may provide a highly promising behavioral link between early-emerging depression and altered brain function.

NAB IN DEPRESSION ONSET AND RECURRENCE

NAB, or increased attention to negative relative to positive information, is posited to play a key role in depression onset and recurrence by increasing the likelihood that depressed individuals will preferentially attend to, process, and fail to disengage from negative stimuli (Beck, 2008). More specifically, NAB increase negative attentional engagement and diminish opportunities for engaging with available positive experiences. Stimulus interpretation and memory are proposed to be similarly biased, with negative features of an event or stimulus being more readily perceived and later remembered given their enhanced perceptual salience (Ellis, Wells, Vanderlind, & Beevers, 2014). Thus, multiple interconnected biases are thought to perpetuate a recurrent cycle of dysphoric affect and diminished positive emotion in depression, with NAB as a purported focal point of this biased information-processing stream. Importantly, this suggests that if NAB can be successfully altered, other positive changes within this information-processing stream may also follow. Pilot data from our group and published data from others suggest that elevated NAB is related to increased depression severity and heightened risk for depression (Kujawa et al., 2011) in preschoolers (see Figure 16.2), providing preliminary evidence that information processes may be similarly disrupted even at this early age. Given that the preschool period is a time of rapid emotional and brain development, as discussed earlier, it would also suggest that successful NAB intervention may prevent maladaptive information-processing patterns from becoming routinized and resistant to change (i.e., neurobiologically committed) in children at increased behavioral risk for depression or in those already showing early emerging depression (i.e., PO-MDD), critically reducing the potential for chronic or recurrent depressive episodes.

NAB AND ATTENTIONAL DISENGAGEMENT IN DEPRESSION

Importantly, NAB in depression has been found to be distinct from that occurring in anxiety. Whereas anxiety has generally been associated with early vigilance for threat (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van IJzendoorn, 2007), basic research findings have suggested that NAB in depression is likely the product of a failure to disengage attention from negative information once engaged rather than a tendency to more rapidly orient

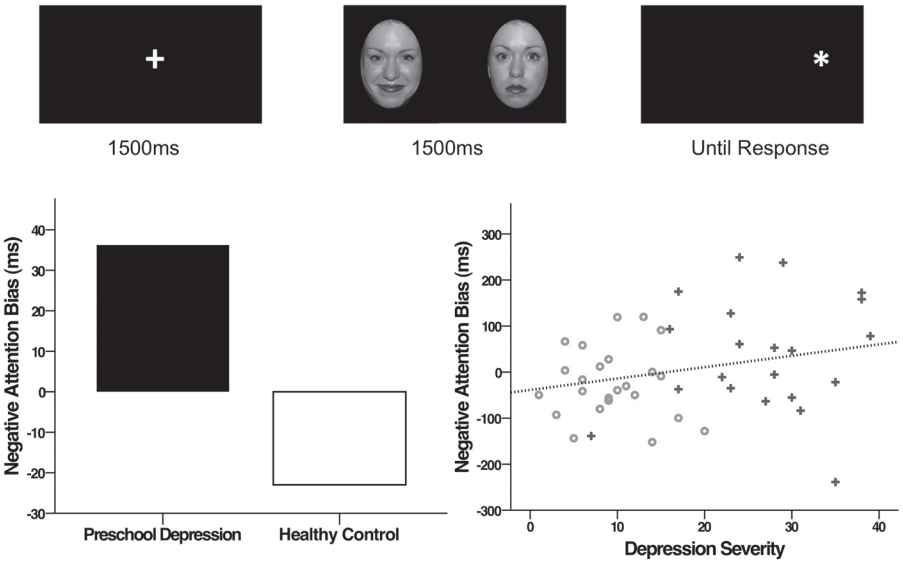

FIGURE 16.2. Negative attention biases are present in preschoolers with depression and are related to depression severity. Following its established usage for identifying attentional biases (Peckham, McHugh, & Otto, 2010), a dot-probe task presented children with two faces at the same time (one on each side of a computer screen for 1,500 ms), followed by one of the faces being replaced by a dot. Face pairs included Sad–Neutral (S-N), Neutral–Happy (N-H), and Sad–Happy (S-H); each pair was presented 15 times during one block (45 trials total); two blocks (90 trials) were administered. Children were required to identify which side the dot was on as quickly as possible using a button press; the dot appeared behind each face type (e.g., happy or neutral) and side (i.e., right or left) with equiprobability. Biases were calculated using a standard approach (see Mogg, Bradley, & Williams, 1995), and incorrect responses and responses below or above a response time cutoff based on previous research (i.e., < 200 ms or > 1,800 ms) were excluded ≥ 60% data remaining was also required). As illustrated in the bottom half of the figure, preschoolers with preschool depression had elevated negative attention biases (measured as S-H; preschool depression $n = 21$, average bias = 36; healthy control $n = 24$, average bias = –23; $t[43] = 1.9$, $p < .05$) and negative attention biases were positively correlated with depression severity ($r[45] = .256$, $p = .04$).

to it (Armstrong & Olatunji, 2012; Gotlib & Joormann, 2010; Koster, De Raedt, Goeleven, Franck, & Crombez, 2005). Interestingly, similar difficulties with disengaging from "relatively" negative stimuli (i.e., reduced attention to, or avoidance of, positive stimuli when paired with neutral stimuli) have been reported as well (Hankin, Gibb, Abela, & Flory, 2010; Joormann & Gotlib, 2007; Joormann, Talbot, & Gotlib, 2007). Identifying that depression affects attentional disengagement (rather than orienting) has proven

critical in defining the specific nature of NAB in depression and supporting its important contribution to disorder onset and recurrence. For example, studies of depression defining NAB as disrupted attentional disengagement have reported associations between NAB and impaired mood (Clasen, Wells, Ellis, & Beevers, 2013) and stress (Sanchez, Vazquez, Marker, LeMoult, & Joormann, 2013) recovery following stress induction. The presence of NAB in individuals at increased risk for depression due to a maternal history of depression (including very young children) (Joormann et al., 2007; Kujawa et al., 2011) and remitted depression have also been reported (Joormann & Gotlib, 2007). Furthermore, research examining the effects of NAB training in healthy individuals suggests the potential for a more direct causal relationship, rather than simply an association, between NAB and disrupted mood regulation. Specifically, healthy adults and children without a NAB prior to training were found to report increased negative mood reactivity following a stressful event only if a NAB had been successfully induced (i.e., training of NAB resulted in mood alterations) (P. Clarke, MacLeod, & Shirazee, 2008; Eldar, Ricon, & Bar-Haim, 2008; MacLeod, Rutherford, Campbell, Ebsworthy, & Holker, 2002). Critically, in addition to providing early evidence for a causative influence of selective attention on emotional reactivity, this early attention training work also highlighted the potential for selective attention to be altered in specific ways using relatively simple training procedures. Recent research adapting these methods for intervention development in adult depression, labeled "attention bias modification" (ABM), have demonstrated highly promising results, suggesting that ABM attenuates NAB in depression and facilitates positive changes in disorder severity and stress reactivity (Browning, Holmes, Charles, Cowen, & Harmer, 2012; Wells & Beevers, 2010).

EVIDENCE SUPPORTING THE THERAPEUTIC POTENTIAL OF ABM FOR DEPRESSION

ABM is suggested to alter NAB by having a given stimulus act in a highly salient, task-relevant manner over successive training trials and sessions (Wadlinger & Isaacowitz, 2011). For example, if a positive stimulus (e.g., happy faces) always acts as an explicit target to be found among other distractor stimuli (e.g., find the happy face among the negative distractors), a habit of automatically directing attention toward positive stimuli is encouraged/learned (i.e., a positive attentional bias is created) (Browning et al., 2012; Waters, Pittaway, Mogg, Bradley, & Pine, 2013). While some negative findings have been reported, likely due to the use of too few training sessions (i.e., one session) and/or inconsistent stimulus–response pairing, well-designed experiments using randomized controlled trial (RCT) methodology (e.g., random assignment, active control) and multiple training sessions have supported the capability of ABM to alter NAB and other important features of depression (e.g., comorbid anxiety). Specifically, NAB and depression severity have

been reported as significantly reduced following ABM in depressed or highly dysphoric adults (Browning et al., 2012; Wells & Beevers, 2010). Notably, more recent work in adults has also shown that reductions in depression severity are maintained for up to 7 months following ABM (Yang, Ding, Dai, Peng, & Zhang, 2015). While not directly targeting depression, in a recent small RCT, Waters et al. (2013), using the ABM approach, reported increased attention for happy faces and reduced anxiety *and* depression severity in school-age children with anxiety following ABM, suggesting that ABM may have beneficial effects on disrupted patterns of attention processing that span features of multiple disorders. Importantly, in a review of 29 available ABM studies reporting data on both attention bias change and emotional functioning, Clarke, Notebaert, and MacLeod (2014) observed that studies reporting positively altered NAB following ABM also reported positive changes in emotional functioning (n = 16), whereas studies with no identifiable changes in NAB following ABM did not (n = 10). Together these findings suggest the significant potential of ABM as a clinical tool, as well as its relevance to very early-emerging depression. However, as detailed below, I also believe they indicate that ABM's potential for use with preschoolers exhibiting very early features of depression (or other related psychopathologies) requires a sound theoretical model that can provide both hypothetical mechanism(s) for how attentional biases are established in the first place and the direct translation of these mechanisms into applied ABM procedures.

COGNITIVE MODELS OF SELECTIVE ATTENTION AND LEARNING PROVIDE A FRAMEWORK FOR HOW ABM ALTERS ATTENTION BIASES, BRAIN FUNCTION, AND DEPRESSION

Dual-processing (DP) models of automatic and controlled behavior suggest that through consistent stimulus–response pairing (i.e., having the same stimulus act as a target over repeated trials), an attentional advantage for a specific stimulus or stimulus feature can be created (Schneider & Chein, 2003; Schneider & Shiffrin, 1977), even in young children (van der Meere & Sergeant, 1988). Based on currently available literature, it is possible that ABM may function in a fashion similar to DP models of stimulus–response mapping. That is, early in ABM training, effortful cognitive control processes are necessary to enhance the perceptual processing (i.e., they increase its perceptual salience) of a targeted stimulus and inhibit processing of distractor stimuli. Once mapping has taken place, attention toward the targeted stimulus and away from distractors becomes more automatic, requiring minimal cognitive effort and becoming highly resistant to stressors (periods of fatigue, stress, etc.), greatly increasing the likelihood of generalization (Fisk & Schneider, 1981; Heuer, Spijkers, Kiesswetter, & Schmidtke, 1998). Importantly, the progression of stimulus–response mapping can be successfully tracked using

averaged response times across training sessions that include training trials varying in number of distracters presented. Specifically, using trials that vary the number of distractor images presented with a target (e.g., three, six, or nine distractor images presented with a single target), search times steadily decrease during early training and eventually stabilize across all trial types, regardless of number of distractor images, once the targeted stimulus–response pairing (i.e., bias) has been successfully established. This provides an explicit operational definition (target search time) and objective measure of response learning (target search time is similar across varying numbers of presented distractor images) and change in attentional control (similar changes in search time across trial types over successive sessions), allowing for the potential identification of an optimal dose (number of sessions required to change) and duration of treatment (number of sessions needed to solidify bias change; see Figure 16.3 for an example of training progress based on the work of Gupta and Schneider (1991) and our pilot work in PO-MDD (Gaffrey, Sylvester, Barch, Pine, & Luby, 2016). Notably, target consistency across trials has been shown to affect significantly the amount of training necessary for establishing a new bias and/or altering an established one, with 100% consistency (i.e., the to-be-trained stimulus is the target on every trial; it is referred to as "consistent mapping" in DP models) critical for the transfer from controlled to automatic attentional processing (Schneider & Chein, 2003).

EFFECTS OF ABM ON BRAIN FUNCTION

Though few available neuroimaging studies directly inform brain changes associated with ABM, recent neuroimaging data in healthy and anxious adults suggest that activity in cortical regions important for regulating attention (e.g., ventrolateral prefrontal cortex [vlPFC]) and visual processing (e.g., visual cortex) change in the expected directions (e.g., increase in vlPFC when shifting attention) following attention training, potentially indicating that attention training facilitates lasting changes at the level of behavior *and* brain function (Browning, Holmes, Murphy, Goodwin, & Harmer, 2010; Clarke, Browning, Hammond, Notebaert, & Macleod, 2014; Eldar & Bar-Haim, 2010). Other studies including anxious adults have reported similar changes in brain function following ABM, including reduced right- and left-amygdala, insula, and subgenual anterior cingulate activation, as well as increased PFC and visual cortex activation (Taylor et al., 2014). Although this work suggests that ABM might influence frontal–amygdala function, the results are difficult to interpret due to lack of either a baseline scan (Browning et al., 2010) or an ABM control group (Taylor et al., 2014). A more recent study examining both neural and behavioral predictors of social anxiety symptom reduction following ABM or a matched placebo-training paradigm has provided some additional clarity (Britton et al., 2015). Specifically, greater left-amygdala activation in response to a threat bias contrast at baseline was associated

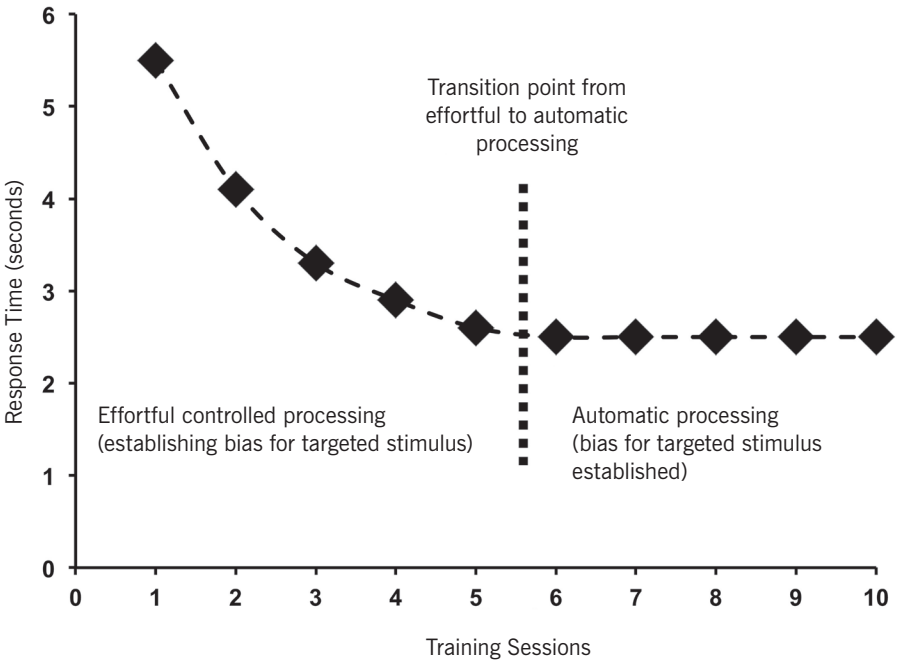

FIGURE 16.3. Hypothesized course of change in bias (measured as response time) and search strategy during attention bias modification training.

with greater symptom reduction across both training groups. However, after accounting for baseline amygdala activation, greater symptom reduction in the active ABM group was found. These findings have important implications for the developm use of ABM in very young children. Specifically, rather than working to positively alter mood through changes in top-down cortical control of emotion, ABM may utilize bottom-up processes implicitly to positively alter biased attention. In line with the DP model of attention and IS model of developing brain function, this would suggest that changing the perceptual salience of a given stimulus has far-reaching effects on attention and the brain function supporting it. Developing a deeper understanding of the underlying mechanisms of ABM may help to optimize this treatment approach and identify those most likely to benefit, potentially including preschool-age children with exaggerated amygdala activation.

ABM THEORY OF CHANGE IN DEPRESSION

A large body of research investigating DP models of automatic and controlled behavior demonstrates that attentional advantages (e.g., increased attention

toward a trained target) transfer across members of a shared category (i.e., are not specific to trained exemplars) and into novel contexts (e.g., persist with novel distractors) once they are learned (commonly referred to as "transfer of training effects"; Schneider & Chein, 2003; Shiffrin, Dumais, & Schneider, 1981). Thus, ABM-induced changes in NAB should generalize outside of the training environment, facilitating attentional engagement with positive experiences and emotion encountered in daily life. As has been previously suggested (Wadlinger & Isaacowitz, 2011), this likely represents the mechanism underlying changes in depression-relevant outcomes following ABM. Specifically, ABM may create an alternative bias (e.g., positive attention bias) that effectively competes with attentional processing "as usual" in depression (i.e., NAB), allowing positive information to selectively capture and hold attention at a much higher rate than the prior status quo. Over time, positive change across multiple levels of information processing and physiological reactivity unfold as positive experiences accumulate, attenuating the acute experience of depression and reducing risk for future recurrence. Though long-term follow-up studies of ABM are still few in number, the currently available data do appear to support this possibility (Wadlinger & Isaacowitz, 2011; Yang et al., 2015). As a result, and in line with the previous discussion, future studies of ABM in early-emerging depression and other, related conditions are likely to benefit significantly from attending to the various ways that social–emotional contexts can influence motivation, treatment adherence, and treatment response.

ABM AND NAB CHANGE IN PO-MDD: AN ILLUSTRATIVE EXAMPLE

Based on our previous discussion of how DP can inform ABM, and to examine whether ABM might be successfully used in preschoolers with depression, we developed and tested a touch-screen version of ABM based on previous work in pediatric anxiety (Waters et al., 2013). Specifically, faces were presented in a 3 × 3 matrix (see Figure 16.4), requiring children to find and touch the one happy face among eight other negative distractors (sad and angry faces) as quickly as possible, over 160 trials. Only one distractor type was used per trial, and angry faces were included, based on a previously successful RCT of ABM in depressed adults using both sad and angry faces (Browning et al., 2012). We subsequently piloted this approach in three children with PO-MDD. Study personnel administered 10 ABM training sessions to each child in his or her home over the course of 3–4 weeks. Each training session included 160 search trials and took place on separate days. Prior to and following ABM training, children completed a touch-screen version of the dot-probe task in their home during separate sessions. As can be seen in Figure 16.5, the preschoolers successfully completed each training session and showed a steep decrease in search times across sessions, potentially indicating a switch from controlled to more automatic search processes as described in

- Matrix search adapted from Waters et al. (2013).
- Child finds the happy face among negative distractors: 160 trials split into three blocks (60, 60, 40) with breaks in between and brief reinforcement (firework display) after each block.
- Delivered over 10 training sessions in the child's home with study staff using a touch-screen tablet and custom-made stand.
- Children are able to earn a prize or activity for completing each training session.

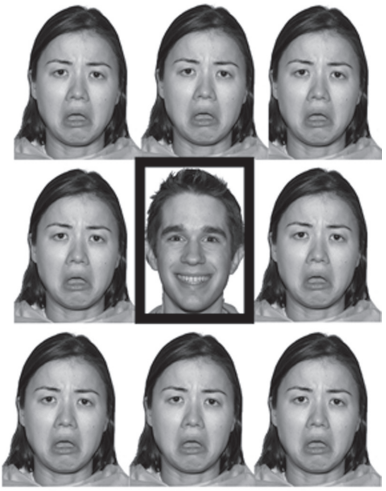

FIGURE 16.4. Attention bias modification procedure for preschool depression. Images from the NimStim Face Stimulus Set are reprinted by permission.

Figure 16.3. In addition, to examine transfer of training effects, the dot-probe task was administered prior to and following ABM training. As illustrated in Figure 16.6, each child demonstrated a bias away from happy faces (reflected as negative bias scores in Figure 16.6) prior to ABM. Following ABM, each child exhibited a bias toward happy faces (reflected as positive bias scores in Figure 16.6) and away from negative faces (reflected as negative bias scores in Figure 16.6), indicating positive attentional changes in the expected directions following ABM, and as would be predicted by DP models of attention and

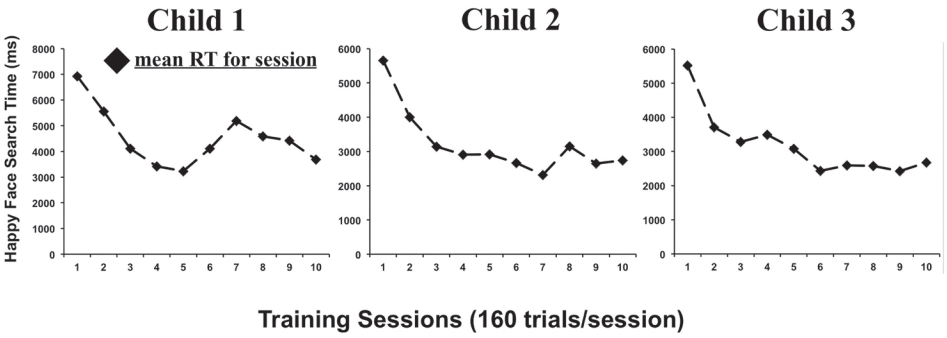

FIGURE 16.5. Individual attention bias modification training curves for three preschoolers with depression.

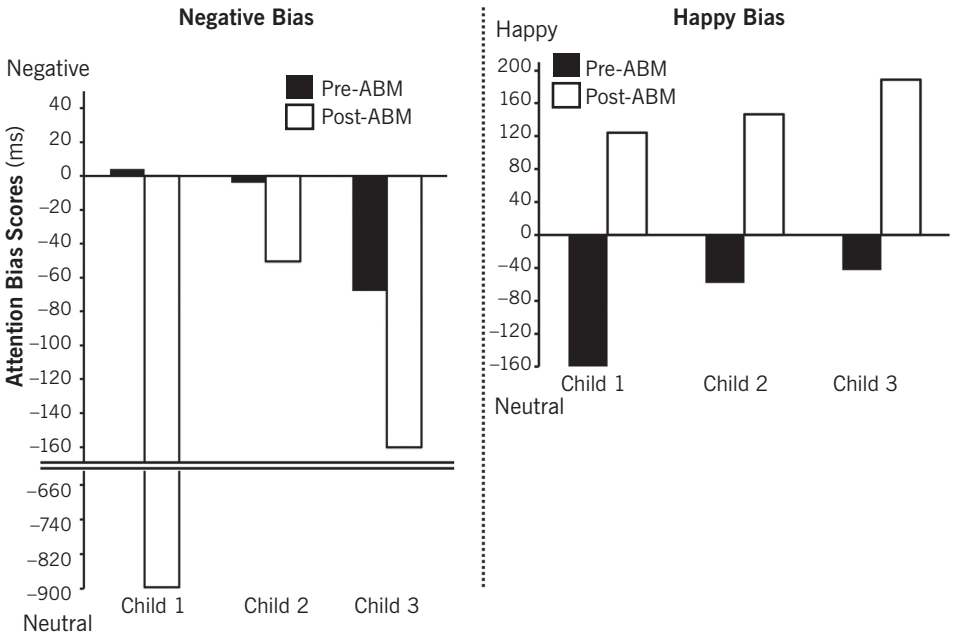

FIGURE 16.6. Attentional biases measured using the dot-probe task pre- and post-ABM training in three preschoolers with depression. Positive attentional bias scores indicate greater attention toward negative or happy faces relative to neutral faces.

learning and previous work in pediatric anxiety (Waters et al., 2013). Though this small pilot of ABM in PO-MDD does not allow any strong conclusions, it does illustrate that ABM procedures can successfully engage preschool-age children, that multiple training sessions can be completed over the course of 3–4 weeks, and that ABM shows promise as an intervention that can successfully alter attentional processing and NAB in PO-MDD and other, related conditions. Nevertheless, much work remains to be done before it is determined whether ABM is a feasible, low-cost, and accessible intervention for PO-MDD that can positively alter current and future (neuro)developmental trajectories of social–emotional functioning in childhood depression.

FUTURE DIRECTIONS

Interpreting whether brain function in members of a clinical group is deviant or disordered is dependent on an understanding of what the expected "normative" values or patterns should be. However, it is also important to determine whether identified differences are representative of a deviant trajectory of

development for a given brain region(s) or network(s), a delay of the expected normative pattern of development, or a pattern of normative development followed by deviation. Critically, the distinction of deviant, delayed, or some combination thereof is critical for informing the form of an intervention (additional practice of a skill, changing the perceptual salience of a given stimulus class, etc.) and whether an intervention has successfully engaged and positively altered its identified neurobiological target(s). This information is also key to investigations of how early intervention alters the interactive processes hypothesized by the IS model, because determining the nature of a given difference and interpreting how it changes following intervention can only be answered in light of data informing the normative brain development process. Thus, future work examining normative patterns of brain development using longitudinal methods is needed to establish a foundation for early intervention development and studies of depression and developmental psychopathology more broadly.

In line with a developmental psychopathology perspective (Cicchetti & Curtis, 2006), future studies of how models of brain development can inform early interventions should take a multilevel and integrated approach. More specifically, the types of experiences likely to influence brain development may be specific to a developmental period of interest, such as parenting (Belsky & de Haan, 2011) and stressful experiences early in life (Casey et al., 2011). As such, it is important to keep in mind that both genes and environment have a hand in guiding brain development, and that including these factors will be critical for developing a fully integrated neurobiological model of early intervention for depression and any other early-onset form of psychopathology. In line with this, early work suggests there may be benefit to combining ABM with other traditional forms of psychotherapy, such as cognitive-behavioral therapy (Shechner et al., 2014). While traditional techniques of cognitive-behavioral therapies are generally not developmentally appropriate for preschool-age children, the combination of ABM with other psychosocial therapies successfully used to treat early-emerging psychopathology (Luby, Lenze, & Tillman, 2012) may have similar benefits. Future work will be required to explore this possibility.

CONCLUSIONS

To date, the advances learned from neuroscience have generally not been integrated into treatment development for early-occurring psychopathology. This is understandable given the complications of conducting neuroimaging research in young children and the challenge of interpreting these findings in light of few data informing the process of brain development. However, as neuroimaging research in young children and across development more broadly continues to grow, neuroimaging data are likely to assume a unique place in the development of early preventive interventions. Specifically,

because neuroplasticity is now understood to represent a core aspect of human development, any attempt to understand how intervention influences behavior will remain incomplete until it charts how brain development modulates such influences. Clearly, such developmental research will vitally inform basic understanding of behavior stability and change more broadly as well. However, since most mental and cognitive disorders begin early in life, such developmental research will undoubtedly be central to our efforts to most powerfully improve the health of children with early-emerging psychopathology. This chapter presents one attempt at integrating theories and empirical data spanning early development and neuroscience, in order to inform a potential path of treatment development that may inform such questions. Data emerging from this or similar models (Bar-Haim & Pine, 2013) are likely to significantly shape the development of future early interventions for preschool psychopathology.

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