CHAPTER 18

Autism Spectrum Disorder

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Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by deficits in social communication and reciprocal social interaction, accompanied by restricted interests and repetitive behaviors (American Psychiatric Association, 2013). While deficits in reciprocal social interaction and the presence of repetitive behaviors define the disorder, difficulties with motor skills, sensory sensitivity, and emotional regulation are very common and clearly impact functioning and response to intervention.

Recent years have seen a dramatic increase in studies investigating the earliest manifestations of ASD and attempting to discern developmental pathways that may characterize the disorder and predict differential outcomes. Much of that research has focused on the study of high-risk infant siblings of children diagnosed with ASD. We begin this chapter with a brief overview of the disorder, followed by discussion of recent research on the earliest manifestations of ASD. In the second half of the chapter we focus on the clinical implications of those findings for early detection, diagnosis, and intervention efforts with infants and young children.

Epidemiology

Current estimates suggest that 1 in 68 children (1.5%) are diagnosed with ASD by age 8 (Centers for Disease Control and Prevention, 2014), with a ratio of 4.5 males to each female. While initial descriptions of the disorder posited a rare condition, ASD is now one of the most common neurodevelopmental disorders. Significant increases in the prevalence of ASD may be partially explained by the broadening of diagnostic standards in DSM-IV (American Psychiatric Association, 1994), which included milder forms of the disorder. In addition, some of the increase likely reflects greater public awareness of the signs of ASD, earlier screening and identification of children at risk, increased availability of intervention services, and substitution of an ASD diagnosis for other categories, such as intellectual impairment. Finally, some real increase in the prevalence of ASD cannot be ruled out (Rice et al., 2012).

Clinical Presentation

Parents typically report concerns with their child's development before the second birthday, often based on delays in communication skills, but the average age at diagnosis in the United States remains shortly after age 4 years (Centers for Disease Control and Prevention, 2012), and later in children from minority backgrounds or low socioeconomic status (SES) (Daniels & Mandell, 2014). Black children are likely to re-

ceive an ASD diagnosis approximately 2 years later than White children, and they are more likely to receive other diagnoses, such as intellectual disability or behavior disorder first (Johnson & Van Hecke, 2015). Notably, several recent studies have investigated racial and ethnic differences in samples with equal access to early screening and evaluation and have revealed that those disparities are no longer apparent when access to evaluation is consistent (Khowaja, Hazzard, & Robins, 2015; Williams, Matson, Beighley, & Konst, 2015).

DSM-5 (American Psychiatric Association, 2013) identifies three areas of deficit in social communication required for diagnosis: (1) deficits in social reciprocity; (2) impairments in nonverbal communication; and (3) deficits in "developing, maintaining, and understanding relationships." In the domain of restricted and repetitive patterns of behavior, interests, or activities, DSM-5 outlines four symptoms, at least two of which are required for diagnosis: (1) repetitive motor movements; (2) inflexible adherence to routines and a need for sameness; (3) restricted interests or intense fixations; and (4) sensory abnormalities, including hyper- or hyporeactivity to sensory input.

Several studies have now documented that the onset of ASD symptoms may be quite variable and that symptoms may emerge at any time between ages 12 months and 36 months (Ozonoff et al., 2015). Some children exhibit a gradual departure from typical developmental trajectories; others appear to develop as expected, then experience a regression in the second year of life (Landa, Gross, Stuart, & Bauman, 2012). Ozonoff and colleagues (2010) described three trajectories in children in the first 2 years: One set of children exhibited early onset of symptoms beginning at about 6 months; a second group appeared to develop normally, then lost skills over time; and a third group appeared to develop normally, then failed to progress during the second year of life.

Equally important, the diagnosis is based on behavioral criteria, and the deficits that define the disorder are indexed by differing behaviors at different ages. In preschool-age children, deficits in reciprocal social interaction include limited efforts to initiate or sustain social interaction, limited capacity for reciprocal conversation, diminished interest in peer interaction, and deficits in developing and understanding relationships. In younger children, these deficits are evidenced by absent or reduced attempts to initiate and sustain joint attention, infrequent affect sharing, limited use of nonverbal communicative strategies (e.g., eye gaze, gesture, social smiling), use of adult hands as a tool, and atypical social approaches. Repetitive behaviors (hand flapping, pacing, waving fingers in front of eyes) are readily observed in some young children with ASD, but there appears to be a subset of children who do not evidence repetitive behaviors until sometime in the third year (Barton, Robins, Jashar, Brennan, & Fein, 2013). Similarly, while restricted interests and insistence on routines are common in preschool-age children with ASD, they can be more difficult to discern in toddlers. Sensory concerns are reported in many children with ASD, but these are also common in children with a variety of other disorders (McCormick, Hepburn, Young, & Rogers, 2016). Similarly, difficulties with emotion regulation are often seen in young children with ASD, but these difficulties are not unique to the disorder. Variability in defining behaviors and in the trajectory of development are now viewed as hallmarks of ASD and have important implications for research, diagnosis, and treatment, which we discuss in later sections of this chapter.

Communication skills also vary widely among children with ASD and may range from significant impairments in functional communication to highly functional and complex language in children of preschool age and older. Even among children with advanced communication skills, however, pragmatic difficulties are common and persistent. Similarly, cognitive skills vary widely in children with ASD. While early studies suggested a high incidence of intellectual disability among children diagnosed with ASD, recent estimates suggest that only 38% of children with ASD function within the range of intellectual disability (Centers for Disease Control and Prevention, 2012). Many of these gains are likely attributable to enormous progress in early identification and early intervention for young children with ASD. Finally, there is an increased incidence of several disorders comorbid with ASD. These include epilepsy, attention deficit disorder, and anxiety and mood disorders.

Outcome

Numerous studies have now documented that early identification of children with ASD and intensive early intervention are associated with significant gains in language functioning and marked decreases in social symptoms (e.g., Sieda et al., 2009). Most children demonstrate

significant gains with intensive treatment, and a few studies have documented that a small number of children appear to improve sufficiently, so that they no longer meet criteria for the diagnosis (Anderson, Liang, & Lord, 2014; Fein et al., 2013). These "optimal outcomes" are associated with intensive early intervention and with slightly diminished severity of initial symptoms (Orinstein et al., 2014). Notably, in the one study to investigate functional magnetic resonance imaging (fMRI) patterns in children who attained an optimal outcome, patterns of brain activation during language tasks remained atypical, suggesting that effective intervention was associated with the development of compensatory neural pathways rather than the normalization of neural mechanisms (Eigsti et al., 2016).

Genetic Markers

While early twin studies were inconsistent in documenting genetic risk for ASD, a more recent study revealed a concordance rate for ASD of 76% among identical twins (Frazier et al., 2014). Notably, identical twins were also likely to have similar severity of ASD symptoms; concordance rates for fraternal twins were 34% for same-sex twins and 18% for different-sex twins. Recurrence risk of ASD in infant siblings of children diagnosed with ASD ranges from 8–20% (Sacrey, Bennett, & Zwaigenbaum, 2015; Szatmari et al., 2016) and is substantially higher than the prevalence rate of ASD in the general population. These data clearly support a genetic basis for the disorder, although genetic mechanisms remain poorly understood. Research has identified more than 100 genes that may contribute to ASD (Dawson & Bernier, 2013) but to date, there is little correspondence between genotype and phenotype (Rapin, 2014; Waterhouse, 2013), except in the case of specific genetic disorders associated with comorbid ASD and intellectual disability, which account for a very small percentage of cases of ASD. More progress has been made in identifying biological markers for ASD.

Biological Markers

Increased cerebral volume at ages 12–15 months (Shen et al., 2013) and reduced connectivity between cortical regions may be early neurobiological features of ASD. Early head circumference studies initially identified atypical growth trajectories and increased head size in toddlers with ASD. While these studies have been criticized for their reliance on outdated normative data for comparison, these early findings have been supported by fMRI studies of brain volume (Hazlett et al., 2005). Several studies have reported enlarged brain volume including both gray and white matter in the temporal and frontal lobes, and in the amygdala in toddlers (Courchesne, Mouton, & Calhoun, 2011; Shen et al., 2013). These findings have been interpreted as a failure of early pruning within specific brain areas.

In a small number of studies, early atypical brain development has been correlated with behavioral symptoms in preschool-age children. For example, brain overgrowth in the amygdala was correlated with impaired joint attention skills in 4-year-old children and with social communication impairments in 5-year-olds (Mosconi et al., 2009; Schumman, Barnes, Lord, & Courchesne, 2009).

In contrast to overgrowth within specific brain regions, researchers have documented significantly reduced connectivity between brain regions, including the temporal, parietal, and occipital lobes in 2-year-old high-risk children diagnosed with ASD (Lewis et al., 2014) and more recently between brain areas that subserve low-level sensory processing (Lewis et al., 2017). Reduced connectivity implies reduced communication between areas of the brain. It is hypothesized that early disruptions to low-level processes derail the development of more complex skills, such as social communication, that require the coordination of multiple brain regions. Researchers have also documented atypical electroencephalographic (EEG) findings and atypical activation patterns on fMRI in children with ASD in the first year of life. There is some evidence that those patterns are associated with observable behaviors (Elsabbagh et al., 2015), and may be altered by early intervention (Dawson et al., 2012). While the data are limited to date, it seems likely that a variety of the neurobiological vulnerabilities that contribute to atypical developmental trajectories as early as the first year of life then result in the behavioral patterns that define ASD.

Early Behavioral Predictors of Diagnosis

The search for early behaviors that might predict diagnosis has been the focus of considerable research. Early studies relying on retrospective

parent report and coding of family videotapes revealed a consistent pattern of few observable deficits at 6 months, followed by a loss of social interest and the development of atypical behaviors between 6 and 12 months (Dawson & Bernier, 2013). By 12 months, children later diagnosed with ASD showed a range of behaviors characteristic of the disorder, including failure to orient to name, reduced social smiling, and social withdrawal. These early studies, while informative, were limited by potential parental recall biases (e.g., regarding onset of symptoms) and conclusions that were based on observations of behaviors in unique situations in which parents were motivated to film their child (Rogers, 2009; Szatmari et al., 2016). In an effort to address these methodological concerns, more recent efforts to identify the earliest signs of ASD have focused on the prospective study of infant siblings of children with ASD.

Studies of High-Risk Infant Siblings

Younger siblings of children with autism are a relatively small group of children at greater than usual risk of the disorder. Following these children prospectively has allowed researchers to investigate early behavioral profiles that indicate risk for ASD and to map trajectories of emerging symptoms (Bryson et al., 2007; Rogers, 2009). We review here key findings from the infant sibling literature regarding early social interaction patterns and atypical motor behaviors that are associated with ASD risk. Throughout, high-risk-ASD infants are infant siblings who eventually developed autism, and high-risk-non-ASD siblings are at risk but do not subsequently develop autism.

Atypical Patterns of Visual Attention

Atypical attentional patterns, particularly in response to social stimuli, are well documented in the first year of life in high-risk infant siblings, and are most often studied using eye tracking devices (see Falck-Ytter, Bölte, & Gredebäck, 2013, for a review). Some studies indicate that high-risk infants later diagnosed with ASD show reduced time looking at people and faces at 12 months of age (Ozonoff et al., 2010), although these findings are not completely consistent (see Guillon, Hadjikhani, Baduel, & Rogé, 2014). Individuals with ASD (and with greater social deficits) spend more time looking at mouths rather than eyes when presented with faces during toddlerhood and adolescence (Jones, Carr, & Klin, 2008), but debate continues about whether these findings apply during infancy. One study indicated decreased fixation on eyes from ages 2–6 months in high-risk-ASD infant siblings (Klin & Jones, 2013), while other studies indicate that high-risk-ASD infants had diminished attention to faces and complex social scenes at 6 months but no relative differences in gaze at eyes versus mouth (Chawarska, Macari, & Shic, 2013; Shic, Macari, & Chawarska, 2014). Researchers posit that while evidence generally supports atypical patterns of attention to social stimuli in high-risk siblings who develop ASD, various factors, including content of stimuli and participant characteristics, contribute to mixed findings (Falck-Ytter et al., 2013; Guillon et al., 2014).

High-risk infants who develop ASD also demonstrate problems with visual disengagement. These children are less likely to disengage flexibly from attention to one object, and this difficulty is predictive of higher Autism Diagnostic Observation Schedule (ADOS) scores at age 2 and potentially later difficulties with arousal regulation and joint attention behaviors (Elison et al., 2013; Elsabbagh et al., 2013; Falck-Ytter et al., 2013; Zwaigenbaum et al., 2005). Alternatively, Jones and colleagues (2016) showed that at 6 months, high-risk infants who later developed ASD demonstrated signs of poor sustained visual attention and disrupted or delayed sensitization to social stimuli (i.e., taking longer to habituate to repeatedly presented stimuli), which suggests that difficulties with the engagement of attention, while common, are highly variable. Research has also revealed potential gender differences in social attention during infancy, with one study showing that high-risk girls demonstrated enhanced attention to social targets (including faces) compared to high-risk males and low-risk males and females (Chawarska, Macari, Powell, DiNocola, & Shic, 2016). Enhanced social attention was predictive of less severe social impairments at age 2 years and may serve as a potential protective factor against ASD in girls. Finally, studies comparing high-risk and low-risk infants (with no data on diagnostic outcome) show that high-risk infants at ages 6 and 11 months demonstrate absence of a left visual field bias when processing faces, a pattern seen in typically developing children (i.e., focusing on stimuli in the left visual field, which projects onto the

right fusiform gyrus). This pattern is posited as a mechanism that facilitates early development of facial processing skills (Dundas, Gastgeb, & Strauss, 2012); its absence may be related to deficits in the processing of facial expressions in children with ASD. Despite the variability in findings, eye-tracking studies have proven very fruitful in identifying behavioral patterns in the second half of the first year of life that predate the more obvious signs of ASD. While the data clearly require replication, they suggest potential neurobiological mechanisms focusing on attention in general, and attention to social stimuli in particular, that may underlie some of the behavioral characteristics of children with ASD.

Social Interaction and Communication

Research with high-risk infant siblings has also identified early signs of social interaction and communication difficulties, beginning slightly later in development. At 12 months, high-risk infants who develop ASD show reduced attentiveness to their mothers during naturalistic interactions and reduced dyadic mutuality; they are less likely to show objects or use directed pointing, and they use fewer and less diverse gestures (reviewed in Sacrey, Bennett, et al., 2015). At 12 months, high-risk infants show poor response to name (Nadig et al., 2007). Compared to low-risk infants, high-risk infants responded less to joint attention probes at ages 12–18 months, which predicted later ASD in several studies (for reviews, see Rogers, 2009; Sacrey, Bennett, et al., 2015). High-risk infants tended to require several pieces of communicative information (e.g., head turn plus verbal communication and gesturing) to improve responding to joint attention probes. High-risk-ASD infants also show reduced coordination of point and gaze at ages 12 and 18 months, and less engagement with the researcher during diagnostic assessments at 12 months (see Jones, Gliga, Bedford, Charman, & Johnson, 2014, for a review).

In addition to delays in nonverbal and gestural communication, high-risk infants who develop ASD demonstrate delays in receptive and expressive language by age 12 months (Landa & Garrett-Mayer, 2006; Sacrey, Bennett, et al., 2015; Zwaigenbaum et al., 2005). Tager-Flusberg (2016) provides a review of language-focused risk factors (demographic, behavioral, neural, and environmental) for ASD, and compares risk factors that may contribute to an ASD versus a specific language impairment diagnosis.

Finally, studies examining early temperament patterns in high-risk infants who develop ASD indicate decreased positive affect and increased distress at age 7 months (Clifford et al., 2013) and at 12 months (Zwaigenbaum et al., 2005). These data may reflect children's diminished ability to use contact with caregivers to regulate negative affect.

Motor Atypicalities

In contrast to early studies that focused largely on social communication skills, recent literature has identified consistent patterns of atypical motor behavior during infancy, particularly in conjunction with work on visual attention. Understanding early visual–motor skills offers insight into the formation of "internal models of action" that may facilitate the development of motor and imitation skills, and understanding of others' actions (Landa, Haworth, & Nebel, 2016). Early atypicalities in motor development may also parallel early and continuing problems with executive functioning in high-risk infants (John et al., 2016). Parental concerns about sensory behaviors and motor development as early as 6 months were found to be predictive of an ASD diagnosis at 36 months in high-risk infant siblings (Sacrey, Zwaigenbaum, et al., 2015), highlighting the importance of understanding and monitoring early risk markers in motor development. Fine and gross motor delays at 12–24 months (but not at 6 months) in high-risk infants who later developed ASD have been documented in several studies (Landa & Garret-Mayer, 2006; Leonard et al., 2014; Ozonoff et al., 2010; Zwaigenbaum et al., 2005). Delayed visual reception and gross motor skills were apparent by age 6 months in high-risk infants who later developed severe ASD-related impairments (Estes et al., 2015).

High-risk infants who develop ASD also appear to engage in atypical patterns of object manipulation during play in infancy. At 6 months, high-risk-ASD siblings were shown to engage in less mature object manipulation and reduced grasping activity (Libertus, Sheperd, Ross, & Landa, 2014; Sacrey, Bennett, et al., 2015). At 12 months, some high-risk infants who later receive an ASD diagnosis engage in fewer throwing and pushing behaviors, and more spinning, unusual visual exploration, and rotating motions

during play compared to developmentally delayed peers (Ozonoff et al., 2008; Rogers, 2009). Researchers hypothesize that early difficulties with effectively and efficiently gathering information about one's surroundings through object exploration may indicate risk for later learning difficulties, diminished social engagement, and continued motor delays (Koterba, Leezenbaum, & Iverson, 2014). In support of this view, Landa, Haworth, and Nebel (2016) found that as early as 6 months, high-risk infants showed less appropriate anticipatory motor responses to a reciprocal social game (i.e., moving the arm/hand to intercept a ball rolled back and forth with a partner).

High-risk infants also demonstrate slower development of skill in sitting and standing postures, postural instability (decreased duration of postures), and pronounced head lag when pulling to sit during the first year (Nickel, Thatcher, Keller, Wozniak, & Iverson, 2013; Sacrey, Bennett, et al., 2015). Again, researchers posit that difficulties learning and utilizing new postures can limit infants' ability to interact with their social environment (Nickel et al., 2013).

Early signs of atypical motor mannerisms and sensory responses have also been documented in high-risk infants. High-risk infant siblings who later developed ASD had increased arm waving at 12 and 18 months in one study (Loh et al., 2007), and increased rate, but not types, of stereotyped motor mannerisms at 12 months compared to high-risk siblings who did not receive an ASD diagnosis (Elison et al., 2014). Other authors, however, have failed to document repetitive object use in infancy (Bryson et al., 2007). These findings may indicate that some high-risk-ASD infants fail to regulate and reduce normative motor stereotypies that typically developing infants regulate from 8–12 months of age. Preliminary findings show that high-risk infants, compared to low-risk infants, may demonstrate hypersensitive sensory processing patterns as early as 10 months (Nyström, Gredebäck, Bölte, & Falck-Ytter, 2015), and hyperarousal to emotional stimuli (Wagner, Luyster, Tager-Flusberg, & Nelson, 2016).

Summary of Data from Infant Siblings

Several generalizations emerge from our review of the data on high-risk siblings. First, most behavioral markers predictive of an ASD diagnosis emerge around 12 months of age, and not earlier, with only a few subtle risk markers identifiable at 6 months, including reduced attention to faces and social scenes, and some visual–motor delays or atypicalities. Importantly, many of the latter are not present in all children and may be observed only in the context of specialized assessment (e.g., eye tracking). This may indicate that behavioral patterns (especially social interaction abilities) observed in the first few months of life may undergo significant changes by the first birthday, and that intact eye contact and socially directed smiling and vocalization before age 12 months may not necessarily preclude risk for developing ASD (Szatmari et al., 2016).

Second, there is enormous heterogeneity in the clinical presentation of ASD and likely many different etiological pathways to any behavioral presentation. Numerous authors have noted that it no longer makes sense to discuss ASD as a unitary concept; instead, clinicians and researchers must consider multiple autisms that differ in etiology and course in ways we do not yet fully understand. Despite considerable effort, research has not yet delineated distinct subclasses of ASD (Waterhouse, 2013). Nonetheless, it seems clear that etiological theories that posit central deficits such as embodied cognition (Eigsti, 2013), weak central coherence (Happé & Frith, 2006), and executive functioning deficits (Van Eylen et al., 2016), may account for a subset of cases of ASD and may eventually help develop intervention efforts tailored to specific vulnerabilities, but they are unlikely to define central etiologies common to most children with ASD.

Third, the literature on early sensory and motor atypicalities in high-risk infant siblings increasingly supports the theory that risk markers of ASD observed during infancy emerge simultaneously across multiple domains of functioning, rather than solely in social-communicative abilities (Rogers, 2009; Szatmari et al., 2016). These findings challenge earlier conceptions of the emergence of ASD as caused by deficits in social motivation. Rather, there may be widespread changes in early brain development involving perceptual, attentional, motor, and social systems and their interaction that increase risk for ASD (Elsabbagh & Johnson, 2016; Jones et al., 2014). That model may account for some of the difficulty devising reliable subclasses of the disorder. Some authors have posited that atypical development may first be evident in motor delays, followed by deficits in attentional control during the second half of

the first year (Brian, Bryson, & Zwaigenbaum, 2015). Both of these sets of deficits may derail early social behaviors such as joint attention and affect sharing. These in turn may contribute to difficulties with emotional regulation and diminished opportunities to engage with and learn about social interaction.

Given that model, it may be most useful to conceptualize behavioral markers of ASD as combinations of features or behavioral patterns rather than domain-specific atypicalities emerging at specific points in time (Szatmari et al., 2016). For example, one study showed that by 18 months, a sample of high-risk-ASD infants could be classified by their symptom presentation into two groups, one with poor eye contact, limited gesturing, and giving of objects to share, and the other with intact eye contact and emerging repetitive behaviors, as well as limited giving, requesting, and sharing (Chawarska et al., 2014; Szatmari et al., 2016).

Despite the advantages of research with high-risk infant siblings, it is unclear to what extent conclusions based on this population can generalize to individuals without familial risk for ASD (Clifford et al., 2013). Findings that rely heavily on parent report may be particularly subject to biases, and repeated assessments may influence the parent's and infant's experiences in ways not well understood (Szatmari et al., 2016). Continuing research with community-recruited samples, directly comparing findings from high-risk-ASD infants and low-risk infants with ASD, and studying other at-risk groups (e.g., low birthweight or preterm infants; Szatmari, et al., 2016) can help answer questions regarding the generalizability of the high-risk infant literature.

It is also unclear whether early behavioral markers identified in studies of high-risk infants are unique to ASD. Some studies have indicated that atypical sustained visual attention is also observed in infants who develop attention-deficit/hyperactivity disorder (Miller, Iosif, Young, Hill, & Ozonoff, 2016). Mitchell, Cardy, and Zwaigenbaum (2011) reviewed studies that compared early risk markers between children later diagnosed with ASD and developmental delay (DD). They found that at 12 months, pronounced social interaction differences and atypical object use and visual exploration distinguished infants with ASD from infants with DD. However, unusual posturing, visual fixations, and repetitive actions did not differentiate infants with ASD. Efforts to replicate this work with high-risk infants and comparison groups of children with other developmental disorders will be important to address these questions.

The data we just reviewed challenged existing models of ASD and prompted significant changes in clinical practices. They have spurred important gains in the ability to identify young children at risk and to provide stable diagnoses of ASD by the age of 24 months and possibly earlier. While early screening and diagnosis clearly promote more consistent access to early intervention services, both have been the subject of some considerable debate.

Early Screening for ASD

There are now several brief, autism-specific screeners in wide use with unselected populations. These include the Modified Checklist for Autism in Toddlers—Revised with Follow-Up (M-CHAT-R/F), the First Year Inventory (FYI), and the Infant–Toddler Checklist (ITC). The M-CHAT- R/F is a 20-item, parent-report screener and a brief follow-up interview designed for use in well-child care settings. Data from several large-scale studies suggest that screening for ASD with the M-CHAT-R/F at 18 or 24 months is quite accurate; the positive predictive value for ASD ranges from .54 to .65, while the positive predictive value for all developmental disorders exceeds .90 (Chlebowski, Robins, Barton, & Fein, 2013; Robins, et al., 2014). Children from minority and low SES families have a higher screen positive rate, but use of the follow-up interview reduces that. Furthermore, diagnoses made after the two-stage screening process do not show demographic disparities, suggesting that universal screening with appropriate follow-up may have the potential to reduce or eliminate demographic disparities in early identification (Khowaja et al., 2015).

The ITC screens for a variety of developmental concerns, focuses on communication, and has been used effectively as an ASD screen with toddlers and preschool-age children (Wetherby, Brosnan-Maddox, Peace, & Newton, 2008). Its authors suggest that since follow-up is required to discriminate children with ASD from children with other developmental disorders, the ITC may be considered a broad-band screener that should be followed by an autism-specific tool. The ITC has recently been tested in 12-month-olds, but the data are as yet inconclusive and suggest that there may

be a high rate of false positives at younger ages (Pierce et al., 2011). The FYI, another parent-report screener, currently in development, is designed for use with children as young as 12 months. While early data suggest that the FYI can identify children at risk for ASD (Reznick, Baranek, Reavis, Watson, & Crais, 2007), data regarding its ability to predict a diagnosis of ASD are not yet available.

The American Academy of Pediatrics recommends ongoing developmental screening through the first 2 years and screening with an autism-specific tool at 18 and 24 months (Johnson et al., 2007). More recently, the U.S. Preventive Services Task Force declined to endorse universal ASD screening, and argued that so far there are insufficient data documenting the relationship between population screening and positive outcomes (Sui & the U.S. Preventive Services Task Force, 2016). Although screening tools are accurate and behavioral treatment is safe, the U.S. Preventive Services Task Force notes that universal screening could lead to provision of services to children who may not have ASD, at significant emotional and financial cost.

Several empirical findings address these concerns. First, although not all children identified by screeners have ASD, nearly all have significant developmental delays requiring intervention (Robins et al., 2014). Second, positive screens must be followed by thorough evaluation for an ASD diagnosis, and these are highly stable by age 24 months, with emerging evidence suggesting stable diagnoses even earlier (Zwaigenbaum et al., 2015). While definitive studies documenting the effectiveness of universal screening are desirable, current data suggest that the benefits of screening outweigh the risk.

Diagnostic Assessment

In addition to widespread screening, there must be clear standards for the assessment of children suspected of ASD and clarity about the diagnosis of the disorder. Diagnostic evaluations should include, at a minimum, information from parents and direct observation of the child. There are several interview-based measures available to solicit information from parents; the most widely used measure is the Autism Diagnostic Interview—Revised (ADI-R). Several studies have noted that while the standard version of the ADI-R is extremely valuable in the assessment of children of preschool age and older, it does not discriminate children with ASD from children with other developmental concerns for those with a mental age of less than 24 months (e.g., Ventola et al., 2006). In response, the authors of the ADI-R have developed algorithms specific to younger children and propose using different cutoff scores for clinical and research purposes. The new algorithm and clinical cutoff resulted in marked gains in sensitivity (Kim & Lord, 2012), and provide more accurate identification of young children based on parental interview.

The Autism Diagnostic Observation Schedule–2 (ADOS-2; Lord, DiLavore, & Gotham, 2012), the most widely used observation tool, now includes five modules: the toddler module for use with children ages 12–30 months, and four advanced modules tied to a child's language level. The ADOS-2 includes a variety of play prompts and "communicative temptations," or tasks designed to elicit communicative efforts from a young child. It is scored in two ways, either by summing items selected for an algorithm and using a cutoff score to determine diagnosis, or by calculating a continuous severity score. Both methods have proven useful in the identification of young children at risk for ASD.

Other observational tools include the Screening Test for Autism in Two-Year-Olds (STAT; Stone, Coonrod, & Ousley, 2000) and the Communication and Symbolic Behavior Scales Developmental Profile (Wetherby & Prizant, 2002). Both of these tools provide observational data designed to discriminate between ASD and other developmental disorders in young children. Finally, there is the Autism Observational Scale for Infants (AOSI), which is a similar set of tasks designed to identify children with autism as young as 12 months (Bryson et al., 2008).

Diagnostic evaluation of children suspected of ASD does not necessarily require the assessment of developmental status, cognitive skills, or adaptive skills, but these can be helpful in assessing strengths and weaknesses, and tailoring intervention. The Mullen Scales of Early Learning (Mullen, 1995) are widely used for the developmental assessment of children suspected of ASD, in part because the scales can be used with children under age 2 years, and because they provide separate subscale scores in the areas of Fine Motor, Gross Motor, Visual

Reception, Receptive Language, and Expressive Language. There are few items at each age level, however, and some data suggest that most children with ASD will receive a *t*-score below 20, which allows for little discrimination in their abilities (Akshoomoff, 2006). Several authors have suggested that age equivalents or developmental quotients may be more helpful than *t*-scores in interpreting test performance on the Mullen Scales (see Yang, Paynter, & Gilmore, 2016). The Bayley Scales of Infant Development—Third Edition (Bayley, 2006) are used to assess children from birth to age 48 months; they include a variety of tasks at each age level and permit highly flexible administration. Clinicians should also include assessment of adaptive skills and sensory issues, both to help in establishing the diagnosis and to address potential impediments to treatment. While these standards reflect considerable consensus in the field about the careful evaluation of young children, there is somewhat less agreement about the criteria for a diagnosis of ASD.

Diagnostic Classification Systems

At present, there are several diagnostic systems that identify children with ASD. The most widely used system in the United States is DSM-5 (American Psychiatric Association, 2013). The DSM was revised in 2013 and includes several significant changes to previous versions. The authors eliminated subcategories of ASD based on evidence that they could not be reliably discriminated and tightened diagnostic criteria to require more pervasive signs of social impairment and the clear presence of restricted interests and repetitive behaviors.

Several studies applied the new criteria to previously diagnosed young children and determined that as many as 29% would no longer meet criteria for an ASD diagnosis, and would therefore be ineligible for autism-specific interventions (Barton et al., 2013; Christiansz, Gray, Taffe, & Tonge, 2016; McPartland, Reichow, & Volkmar, 2012). This was especially concerning because young children who presented with less significant impairment, and often received a diagnosis of pervasive developmental disorder not otherwise specified (PDD-NOS) in earlier DSM versions, responded especially well to early intervention and attained the most positive outcomes (e.g., Moulton, Barton, Robins, Abrams, & Fein, 2016).

The *International and Statistical Classification of Disease and Related Health Problems* (ICD-10), published by the World Health Organization (WHO; 2011) is the diagnostic system used by most of the world outside of the United States; a revision is expected sometime in 2018. ICD-10 retained several subcategories of ASD diagnoses, including childhood autism and Asperger syndrome. It also includes atypical autism for those children who do not meet standard criteria by virtue of either their age or symptom presentation, or both.

In 2016, Zero to Three published the third edition of *Diagnostic Classification of Mental Health and Developmental Disorders of Infancy and Early Childhood: DC:0–5,* which focuses on developmental considerations appropriate to the diagnosis of young children. DC:0–5 retains the category of ASD as described in DSM-5, but it adds additional developmental specifiers.

DC:0–5 also includes a second disorder, early atypical autism spectrum disorder (EA-ASD), which is intended to identify children ages 9–36 months who do not meet full criteria for ASD but do present significant symptoms and impairment (Zero to Three, 2016). The justification for the new disorders is the considerable data on early signs of risk for ASD in infant siblings (Soto, Kiss, & Carter, 2016). The goal is to provide intervention to young children who exhibit signs of impairment but do not present the full pattern of symptoms consistent with a DSM-5 diagnosis. The new DC:0–5 system offers an opportunity to collect data about the specific clinical presentation of ASD in young children. While we await these data, it seems critical that clinicians identify children as early as possible and advocate to provide intervention services to very young children who present subclinical impairments consistent with ASD.

Intervention

Evidence that intervention is most effective when it is initiated early in development has prompted efforts to develop intervention models suitable for use with younger children. In addition, data from baby sib studies suggest that intervention may be viewed not simply as a way to teach skills, but as an effort to offset negative trajectories and reestablish more typical developmental pathways (e.g., Dawson, 2008). There is a considerable literature documenting the effectiveness of applied behavioral analysis, in-

cluding discrete trial instruction for preschool-age children (see Reichow, 2012, for review), but recent efforts have focused on expanding these models, especially to younger children. Schriebman and colleagues (2015) reviewed the development of second-generation behavioral intervention models from the earliest discrete trial models, and noted that while behavioral models are effective in teaching specific skills, there have long been concerns with the failure to generalize skills learned in one setting to novel contexts, with difficulties engaging children in treatment, with a lack of spontaneity in language, and with excessive dependence on prompts.

In addition, Schriebman and colleagues (2015) and Dawson and Bernier (2013) highlight core principles emerging from research in developmental science that have shaped approaches to intervention with young children. These include the importance of prelinguistic skills, including gesture, imitation, and joint attention in facilitating language development and social communication, and the recognition that young children are active learners who learn best in the context of self-initiated exploration of their environment and affectively rich social relationships. In response to these data, multiple researchers have created intervention programs that imbed behavioral methods in child-initiated activities, include a focus on natural rather than arbitrary contingencies, and provide intervention in more naturalistic and developmentally sensitive settings and in the context of naturally occurring routines. These models, called "naturalistic developmental behavioral interventions" (NDBI) have been associated with more rapid acquisition of skills and with significant gains in the generalization of skills (Dawson & Bernier, 2013). They appear to be especially useful with young children because of the flexibility of the model, and because young children are less likely to have firmly entrenched negative behavior patterns. These models include the Early Start Denver Model (Rogers & Dawson, 2010); the Social Communication, Emotional Regulation, and Transactional Support model (Prizant, Wetherby, Rubin, Laurent, & Rydell, 2005); pivotal response treatment (Koegel & Koegel, 2006); joint attention, symbolic play engagement, and regulation (Kasari et al., 2014); and others. We review a small sample of representative models here.

Koegel and Koegel (2006) developed pivotal response therapy to focus on teaching critical skills (e.g., social initiation) that might underlie functioning in multiple areas. Therapists use behavioral strategies, but they rely on natural reinforcers and use child preferences and child-initiated activity, often in the context of naturally occurring routines. Pivotal response therapy has a significant base of empirical support and has demonstrated effectiveness in increasing targeted skills such as social initiation and in increasing nontargeted skills such as pretend play and imitation in preschool aged children (Ingersoll & Schriebman, 2006). Other early adaptations of behavioral methods focused on specific skills such as joint attention, which were believed to support early communicative efforts. Kasari, Paprell, Freeman, and Jahromi (2008) reported on a randomized controlled trial of an intervention designed to increase joint attention skills in preschoolers; the preschoolers demonstrated significant gains in joint attention and play skills, as well as more rapid language acquisition in the treatment group.

Dawson and colleagues (2010) provided data from the first randomized controlled trial of a comprehensive intervention program for children under age 3 with ASD. The Early Start Denver Model combines a developmentally informed curriculum focused on affective communication and child-directed activities, integrated with behavioral principles. The authors provided 4 hours of intervention daily for up to 2 years to children diagnosed with ASD between the ages of 18 and 30 months. They reported significant gains in IQ scores and adaptive behaviors, and marked reductions in ASD symptoms in children in the experimental group compared to children who received community-based treatment. Treatment effects were moderated by the children's ages and the intensity of services, such that children who enrolled in the program at younger ages and received more intensive services attained better outcomes. The Early Start Denver Model also includes parent training; parents were provided an additional 16 hours of services weekly.

Several recently developed NDBI for young children have focused on parent training and parent mediated intervention. These models train parents to develop reciprocal communication patterns and to respond consistently to child overtures and behavior. Parents provide many hours of supportive interaction daily, largely within the context of naturally occurring routines. The training may also help parents develop more gratifying interactions with

their children with ASD, which may contribute to efforts to redirect developmental trajectories.

Rogers and colleagues (2014) tested a parent-implemented version of the Early Start Denver Model with seven infants ages 6–15 months who presented early signs of ASD on the AOSI. Intervention consisted of one session weekly of parent coaching for 12 weeks, with careful assessment of treatment fidelity. At 36-month follow-up, the treated group presented lower rates of ASD and of developmental quotients below 70 than a group of children who had been less symptomatic at 9 months and whose families declined treatment. Only two of the seven children in the experimental group received an ASD diagnosis at 36 months. Equally important, parents learned intervention strategies designed to increased parental responsiveness and enhance parent–child interaction. These data are limited by a small sample size, lack of random assignment, and the possibility that parents of high-risk siblings may be especially motivated to engage in intervention efforts; nonetheless, they suggest that a low intensity, parent-implemented intervention may be helpful to some families and that intervening before a clear diagnosis of ASD is established may alter negative developmental trajectories.

Wetherby and colleagues (2014) reported on a randomized controlled trail of the Early Social Interaction Project for children ages 16–20 months with ASD, which investigated the intensity of parent coaching needed to support effective treatment. Children were randomly assigned to individual parent coaching or group coaching, both of which focused on increasing social communication. Children in the individual treatment group demonstrated gains on observation-based measures of receptive language and social communication and on parent report measures of communication and social skills, compared to children in the group coaching program. The authors suggest that for parent-implemented models to be effective, parents must be provided with individual coaching and support. Similarly, Brian and colleagues (2015) reported on a 12-week clinical trial of an adapted version of pivotal response therapy with infants. They provided in-home parent-mediated interaction with coaching from an interventionist. The authors reported that infants demonstrated gains in language performance and verbalization, as well as increases in imitation, social orientation, and social responsiveness.

Based on their review of the literature, Schriebman and colleagues (2015) and Zwaigenbaum and colleagues (2015) offer a series of recommendations for intervention with young children with ASD. They argue that intervention should begin as early as possible and include integrated behavioral and naturalistic strategies. Services should involve parents and caregivers actively and include systematic training and education, as well as ongoing individualized support for parent-mediated intervention. Intervention should focus on multiple features of ASD, including social communication, emotional regulation, sensory concerns, motor difficulties, and negative behaviors, and it should begin with attention to prerequisite skills such as joint attention, affect sharing, and play. Clinicians should consider each family's social and cultural context, and tailor services as much as possible.

Future Directions

Despite considerable progress in the field of ASD, many questions remain. The heterogeneity of ASD is clearly recognized, but research has made limited progress toward identifying potential subgroups or different developmental trajectories. Large-scale studies that assess behavioral patterns, as well as neurological and neuropsychological findings, will be important to disambiguate the complex heterogeneity of ASD. These efforts might permit the development of interventions tailored to specific behavioral profiles, and may help identify moderating variables that explain individuals' differential responses to treatment.

Intervention research has clearly made enormous progress in recent years, especially in interventions with young children, but there is much still to be done. Direct comparison of intervention models in randomized controlled trials have been rare and might help identify the critical ingredients of effective treatment. Early studies suggested that intervention must be very intensive; more recent studies have suggested that less intensive models may also be effective, particularly when they include well-supported parent intervention. But this is unlikely to be true for all children and families, and it is unclear when more intensive services are required to effect change. Researchers must engage diverse samples of participants and should pay careful attention to the assessment of treatment

fidelity, especially as parent-mediated models become more common; more data are needed regarding how parent training and support is best provided. All of these goals must be supported by the more consistent use of outcome measures sensitive to changes in prerequisite skills and emerging capacities (Zwaigenbaum et al., 2015).

Finally, researchers must consider the application of intervention strategies developed in highly controlled settings to the real-life contexts in which they will be used. Too often, a significant "research to practice gap" (Dingfelder & Mandell, 2011) confronts clinicians who struggle to implement empirically supported assessment tools and intervention models in community settings and in culturally sensitive ways. Despite clear guidelines for the assessment of children with ASD, community-based assessments are highly variable and often require long waits. In 2007, 22% of states listed no formal requirements for diagnostician training, and only 7% required that professionals use specific tools (Stahmer & Mandell, 2007). Similarly, empirically supported intervention models are not readily available in community settings (Hess, Morrier, Heflin, & Ivey, 2008), and there is limited understanding of how interventions might be tailored to cultural considerations. While parent-mediated interventions offer great promise, families affected by poverty, trauma, substance abuse, and mental health concerns may struggle to implement these models with the fidelity they require. Innovative models that blend infant mental heath services with autism-specific interventions are needed and will require cross-training of professionals from multiple disciplines.

Continued struggles to fund early intervention services must also be addressed. Services for children under the age of 3 are typically provided by state-funded early intervention programs, with limited federal support from Part C of the Individuals with Disabilities Education Act (IDEA; 2004). Currently, 44 states include autism as a criterion for eligibility for early intervention services, but definitions of ASD vary (Barton et al., 2016). Some states have developed guidelines for the content and intensity of services for children with ASD, but few specify the use of empirically supported intervention models or NDBI, and most recommend eclectic models, despite a lack of empirical support for those (Boyd, Odom, Humphreys, & Sam, 2010). Once children turn 3, responsibility for intervention shifts to local school systems, which are typically funded by property tax revenues. This results in significant disparities between states and between communities, with markedly fewer resources available in impoverished communities. As a result, public educational settings may not use recommended practices and instead use lower-intensity interventions (e.g., Downs & Downs, 2010; McLennon, Huculak, & Sheehan, 2008). Effective intervention requires trained staff, consistent implementation and evaluation of progress, attention to model fidelity, and ongoing family support. The provision of high-quality treatment to young children with ASD is challenging and complex, especially in an era of fiscal restraint. Nonetheless, the evidence is clear that investment in the timely identification and treatment of young children with early signs of ASD will save money in the long term; more important, it has the potential to shape evolving developmental pathways toward much more positive outcomes for children and families.

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