Autism Spectrum Disorders in infancy and toddlerhood: A review of the evidence on early signs, early identification tools, and early diagnosis

Josephine Barbaro, BBSc (Hons) and Cheryl Dissanayake, PhD

Olga Tennison Autism Research Centre
School of Psychological Science
La Trobe University
Bundoora, Victoria, 3086
AUSTRALIA

Phone: +61 3 9479 3271
Fax: +61 3 9479 1956
Email: j.barbaro@latrobe.edu.au; c.dissanayake@latrobe.edu.au

Corresponding Author: Cheryl Dissanayake, PhD
Address: Olga Tennison Autism Research Centre, School of Psychological Science, La Trobe University, Bundoora, Victoria, 3086, AUSTRALIA
ABSTRACT

To date, the biological basis of Autism Spectrum Disorders (ASD) remains unknown. Thus, identification and diagnosis is reliant on behavioural presentation and developmental history. There have been significant advances in our knowledge of the early signs of ASD through the use of retrospective videotape analysis, parental report, screening studies, and more recently, studies of high risk infant siblings. Despite behavioural markers being identified within the first year of life, the current average age of diagnosis for ASD remains at around 3-years of age or older. Consequently, these children are not receiving intervention in their early years, which is increasingly recognised as an important time to begin intervention. There remains little research on the prospective identification of these children in a community-based sample prior to 18-months of age. It is recommended that future prospective studies monitor behaviour repeatedly over time, thereby increasing the opportunity to identify early manifestations of ASD, and facilitating the charting of subtle behavioural changes that occur in the development of infants and toddlers with ASD.

Key words: autism spectrum disorder; autistic disorder; infancy; early identification; early diagnosis; screening tools
INTRODUCTION

The last decade has seen significant advances in our knowledge of the very early manifestations of Autism Spectrum Disorders, beginning with the use of retrospective home videotapes for the purpose of examining behavioural features in infants who later received a diagnosis of an Autism Spectrum Disorder (ASD). This increasing knowledge of the early ASD phenotype has led to attempts to prospectively identify ASDs in infancy and toddlerhood. Importantly, prospective studies allow the researcher to elicit behaviours at a specific age, rather than relying on spontaneous presentation on videotape, or retrospective parental report. More recently, prospective studies of infant siblings of children with an ASD have also contributed to increased knowledge of the early phenotype.

Despite the unquestioned neurobiological basis of ASDs, limited knowledge regarding the underlying neuropathology for these related conditions has meant that diagnosis is reliant on behavioural presentation and developmental history. Although there now is increasing empirical information on the very early developmental histories and behavioural presentation of children with ASDs, scientific knowledge about the early signs vastly precedes standard practice, with the average age of diagnosis still at around 3-years of age. Thus, the purpose in this paper is to bring together recent advances in the field, including recent research involving ‘high-risk’ infants, to inform practitioners about the very early signs of ASDs, as well as the instruments used to identify these signs, consequently informing their current practice.

Together, this body of work will be reviewed with the ultimate aim of reducing the age at which ASDs are diagnosed. Early identification and diagnosis provides the best opportunity for early intervention, which can prevent ASDs from becoming fully manifest in the developing child, thereby serving to maximise developmental outcomes.
Age of onset / recognition of symptoms

Although the Diagnostic and Statistical Manual of Mental Disorders-IV-TR (DSM-IV-TR\textsuperscript{3}) and the International Classification of Diseases-10 (ICD-10\textsuperscript{4}) state that the onset of impairment in Autistic Disorder (AD) must be prior to 36-months, a large proportion of children manifest developmental problems between 12- and 24-months\textsuperscript{5-7}, with some showing abnormalities prior to 12-months of age\textsuperscript{8-15}.

Neither the DSM-IV-TR\textsuperscript{3} nor the ICD-10\textsuperscript{4} specify an age of onset criterion for Asperger’s Disorder (AspD). However, onset in AspD is usually reported to be later than in AD, as these children develop language at an appropriate age and display less severe symptoms. As there are fewer symptoms to alert parents and professionals that development is impaired, AspD is typically not identified prior to children becoming part of a preschool or school setting (i.e., usually after 4-years of age\textsuperscript{16, 17}). Nonetheless, it is possible to identify some (albeit a very small percentage) children with AspD prior to 36-months\textsuperscript{18, 19}. Thus, it is the recognition of impairments in AspD, and not onset, which occurs later than 36-months.

Individuals with Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS), by definition, do not need to have an onset of impairment prior to 36-months\textsuperscript{3-4}. However, this is not typical of most individuals with PDD-NOS\textsuperscript{20}.

INFANT SIGNS OF ASDs: REVIEW OF THE RETROSPECTIVE LITERATURE

Retrospective videotape analyses

Adrien and colleagues were the first researchers to utilise home videotapes to assess the behaviours of children with and without an ASD before and after their first birthday\textsuperscript{8-10}. Using the Infant Behavioural Summarized Evaluation Scale, the key behaviours that differentiated the groups were in the areas of socialisation (ignores people; prefers aloneness; poor social
interaction; no eye contact) and communication (lack of vocal communication; lack of appropriate facial expressions; no social smile; lack of gestures; no or poor imitation of others).

In their study of first birthday videotapes, Osterling and Dawson\textsuperscript{12} found that four behaviours correctly differentiated 90\% of their sample of children later diagnosed with an ASD from those without an ASD. These were a low frequency of looking at others (including eye contact) and orienting to name call, an absence of showing objects, and a lack of pointing. These findings were later replicated\textsuperscript{13,21}. A deficit in orientating to name call has consistently been found to differentiate children with and without an ASD as early as 8-months of age, in both retrospective and prospective studies\textsuperscript{11,15,22}. Interestingly, Osterling\textsuperscript{21} found that while 12-month-olds with an ASD and associated intellectual disability oriented to their names and looked at others less frequently than infants with only an intellectual disability, both groups engaged in repetitive motor actions more frequently when compared to typically developing (TD) infants. Thus, repetitive and stereotyped behaviours may not be specific to ASDs, but associated with intellectual disability; the findings suggest that social attention and communication behaviours are better early indicators of ASDs\textsuperscript{23}.

Observations of home videotapes by Clifford and Dissanayake\textsuperscript{24} revealed that infants later diagnosed with an ASD showed deficits in social smiling and eye contact as early as 6-months of age compared to infants without an ASD. In toddlerhood, affected children showed deficits in initiating and responding to joint attention (JA) behaviours. They found that requesting behaviours were less problematic, indicating that it is the sharing quality of JA behaviours that is deficient in these children, and not the act of requesting attention. Clifford et al.\textsuperscript{25} also found a lack of protodeclarative showing in children with AD compared to TD and developmentally delayed (DD) infants.
Although the use of retrospective home videotapes is an effective means of charting the very early development of children with an ASD, there are limitations to this methodology. Firstly, the behaviours observed are constrained to selective and less naturalistic representations of the child’s behaviour, as the videotapes are usually of the child’s birthday party or a family event, and not of undesirable or unpredictable situations. Furthermore, it is not possible to elicit a desired behaviour, such as response to a social smile, thus limiting observations to behaviours spontaneously demonstrated in the situation\(^{11}\).

**Retrospective parental reports**

Retrospective parental reports have long been used as a source of information about the development of ASDs in infancy. Vostanis et al.\(^ {26}\) requested the parents of children with an ASD, learning disabilities, and language disorders to complete a questionnaire about their child’s development between 12- and 18-months. The children with an ASD were rated significantly lower on items involving social attention and communication, including imitation, pointing at objects, playing peek-a-boo, seeking and enjoying cuddles, checking for their parents, interest in other children, and waving bye-bye without being asked.

Young et al.\(^ {27}\) asked 153 parents of children with an ASD to complete a questionnaire concerning their child’s very early development, and the age of onset of problematic behaviours. Parents were primarily concerned about their child’s difficulties in social awareness and understanding, a lack of shared enjoyment in interaction, and poor eye contact. Little interest in other children, and a lack of social referencing (JA behaviours) were also reported, with 95% of parents indicating that these behaviours occurred before the age of 2-years.

The Early Development Interview (EDI) was recently developed to chart the development of children with an ASD from birth to 2-years\(^ {23, 28}\). The parents of young children
with an ASD, DD, and TD children were interviewed with the EDI regarding various behaviours including social attention and communication behaviours. The children with an ASD were reported to have more social deficits than TD children from as early as 3- to 6-months of age, and more deficits than children with DD at 13- to 15-months of age. Consistent with the retrospective videotape studies, these deficits included poor eye contact, failure to orient to their name, deficits in the use of JA, and little engagement in social interaction. Werner et al.\textsuperscript{23} concluded that social behaviours were the best indicators of diagnostic differences between children with an ASD and TD children, as well as between children with an ASD and DD, albeit at a later age.

Baranek and colleagues\textsuperscript{29-31} developed a parental questionnaire that focuses on the behaviour of children at risk for ASDs prior to 12-months, called The First Year Inventory (FYI). In order to examine the construct validity of the FYI, Watson et al.\textsuperscript{31} developed a retrospective version, and gave this to parents of preschoolers with an ASD, developmental disability, and TD children. The items that were most useful in distinguishing between ASDs and developmental disability were orienting to name call, following a point, social orienting, interest in children his/her age, social smiling, facial expression, playing peek-a-boo, and demanding attention of the caregiver. Items on imitation, expressive communication, sensory processing, regulatory patterns, reactivity, and repetitive behaviours generally differentiated children with an ASD and developmental disability from TD children, but were not good at distinguishing the former groups. Thus, once again, the items that best distinguish children with and without an ASD are located in the realm of social attention and communication.

A limitation of parental report studies is that parents’ responses are vulnerable to incorrect memory recall, recall biases, and distortion of events\textsuperscript{32}. Furthermore, various factors,
including parental alertness in recognising behaviour, socio-economic status, personality, intelligence, and parental mental health can influence their responses, reducing reliability of the data\textsuperscript{33}. However, it is worth noting that the findings from the parent report studies do largely concur with the findings from the videotape studies\textsuperscript{24}.

In addition to the behavioural signs identified by retrospective studies, more recently, biological markers, namely enlarged head circumference, have been investigated as possible signs of ASDs. Although head circumference size is normal or near normal at birth, subsequent accelerated head growth over the first 2 years of life leads to approximately 20\% of children with an ASD having a head circumference above the 97\textsuperscript{th} percentile\textsuperscript{34-36}. Used together with social attention and communication behaviours, head circumference data may be a useful accompaniment when determining the diagnostic status of a child. However, this information must be used with caution as no prospective data have yet been collected to show whether atypical head growth in very early infancy can predict a diagnosis of an ASD\textsuperscript{36}.

**AGE OF DIAGNOSIS**

Despite the accumulating evidence that signs of ASDs are present in early infancy, the interval between many parents’ first concerns and a definitive diagnosis is around 3 to 4 years\textsuperscript{37}. This interval increases to as high as 9 years for those diagnosed with AspD\textsuperscript{27, 38-41}. Recent developments in the early identification field have facilitated lowering the average age of diagnosis for the ASDs, with the average age of diagnosis in the USA being 3.1-years for AD, 3.9-years for PDD-NOS, and 7.2-years for AspD\textsuperscript{37}. However, given that the literature is showing that signs of ASDs are present in the first year of life, the mean ages for diagnosis are still very high, especially for ASDs other than AD. There are a number of reasons for the late diagnosis of ASDs despite their early behavioural manifestations, which are outlined below.
Current diagnostic criteria

A significant limitation to an early diagnosis is the fact that many of the characteristic behaviours currently used in diagnosis of ASDs, based on the DSM-IV-TR\textsuperscript{3} and the ICD-10\textsuperscript{4} criteria, are not apparent before 36-months. These criteria are based on symptoms that are rarely seen in infants and toddlers with ASDs, but are common in older children and adults\textsuperscript{42, 43}. For example, difficulties socialising with peers and deficits in language skills are symptoms that develop later in childhood, and are thus not easily observed in infancy\textsuperscript{14}. Some of the behaviours may also be secondary, developing to compensate for the primary ‘core’ deficits of ASDs, which are those that are seen early in the development of the disorder\textsuperscript{44, 45}.

In addition, the DSM-IV-TR\textsuperscript{3} and ICD-10\textsuperscript{4} require a presence of repetitive behaviours, interests, stereotypies, or rituals to diagnose an ASD. This is problematic when attempting to diagnose very young children, as these behaviours present in only a minority of children prior to 18-months and tend to develop, or become more apparent, at around 3- to 4-years of age\textsuperscript{42, 45-47}. Therefore, the absence of these behaviours in infants and toddlers with social and communication impairments does not exclude the possibility of an ASD\textsuperscript{42}. However, more recently, data suggests that repetitive and stereotyped movements can distinguish between children with an ASD and those with delayed or typical development late in the second year of life\textsuperscript{48}. The focus on behaviours evident later in development inevitably means that the diagnosis of infants and toddlers is delayed. In order to promote early diagnosis, the criteria in current diagnostic manuals require modification to reflect those behaviours that are present in the infancy period\textsuperscript{49}.

Late onset / regression
Although most children with an ASD show problems before 12-months of age, there is a cohort of children who appear to develop typically in the first 15- to 21-months of life. These infants reach appropriate language and social skill milestones, but then progressively ‘lose’ these skills, with the majority losing skills between the ages of 13- to 18-months\textsuperscript{23,50-54}. This ‘regression’ occurs in approximately 20\% of children with an ASD, although this figure has been reported to be as high as 49\%\textsuperscript{51,55-58}. The differing percentages may be an outcome of the diagnostic status of the child, with a recent report\textsuperscript{54} charting the incidence of regression to be highest in those with a diagnosis of AD (as opposed to AspD and PDD-NOS).

The most frequently reported skill loss is language, followed by social skills\textsuperscript{50,55,58}. However, it should be noted that most cases of regression do not involve completely normal development prior to regression\textsuperscript{23,59,60}, with some children having lower language abilities than their TD peers prior to regression\textsuperscript{58,61}. Nonetheless, the existence of regression in a subset of children with ASDs means that professionals must remain cognizant of this group of children. If this period of regression remains unrecognised, diagnoses may be unnecessarily delayed.

**Language development**

It is usually the absence of typically developing language, which becomes evident at about 2-years, that leads to children being referred and diagnosed with an ASD\textsuperscript{62}. Delay in language development is one of the first and most frequently expressed concerns of parents of children later diagnosed with an ASD\textsuperscript{5,27,40}. It is thus not surprising that delays in referral are seen when a child is verbal, and are exacerbated when the child does not have associated intellectual disability. These children usually receive a diagnosis of AspD, which, as previously mentioned, is diagnosed much later than AD\textsuperscript{16,17}. Indeed, Mandell et al.\textsuperscript{37} found that children
with severe language deficits received a diagnosis of an ASD 1.2 years earlier than children with less severe language deficits.

**Knowledge of infant symptoms**

Most general practitioners and paediatricians do not have specialised skills or training regarding ASDs in infancy. Consequently, they do not possess sufficient clinical expertise to identify the subtle symptoms of ASDs in infancy, and often attribute any abnormalities to general developmental problems. Too often, parents are reassured by their physician and told “not to worry”, and that “they’ll grow out of it”. Howlin and Asgharian, studying over 770 families in the UK, found that over a quarter of parents of children with AD and a third of parents of children with AspD were reassured that their child was developing normally. The average age of the children with AD when parents first sought help was 2-years, and with AspD, 3.5-years; yet, on average, a diagnosis was given at 5.5-years of age for the children with AD, and 11-years of age for the children with AspD.

What is most concerning is the lack of familiarity amongst practitioners with the tools to identify ASDs. Wiggins et al. found that 70% of practitioners do not use a diagnostic instrument when assessing for an ASD. Furthermore, Dosreis et al. found that 82% of the paediatricians sampled screened for general developmental delays, but only 8% screened for ASDs. The main reason cited was lack of familiarity with specific tools for ASDs (62% of respondents).

Even in toddlerhood, many physicians are not recognising the signs of ASDs, and are unnecessarily delaying diagnosis. As a consequence, children with an ASD are not receiving intervention in their critical early years.
IMPORTANCE OF EARLY DETECTION AND DIAGNOSIS

Early identification of the signs of ASDs is the first step to facilitating early referral and diagnosis. Early diagnosis provides the best opportunity for early intervention, which serves to maximise developmental outcomes for affected children and their families. It is widely recognised that the earlier intervention begins in a child’s development, the better the opportunities to move the young child toward a more typical developmental trajectory, due to the plasticity of the young brain\(^1,69\). However, few studies have investigated the efficacy of intervention prior to 2-years of age, and there continues to be a need for more Randomised Controlled Trial (RCT) studies in this area\(^1,70,71\). Despite this, the results from these few studies, including those that use case reports and single-subject designs, are promising\(^1,71-78\).

Importantly, the onset of secondary (compensatory) behaviours may be prevented, or at least minimised, with early intervention\(^27,45\). Furthermore, if a child is referred before a ‘drop off’ in language and social skills, the impact of early intervention is even greater, as it may prevent some of these losses\(^1\). Mundy and Crowson\(^79\) proposed a ‘cybernetic model’ of ASDs, whereby an Initial Pathological Process (IPP; i.e., a decrease in attending to and processing social stimuli) feeds back upon itself over the first 2-years of life, resulting in a Secondary Neurological Disturbance (SND; i.e., resulting in secondary deficits of ASDs). They argue that without early intervention, the effects of SND push the child with an ASD further away from the path of typical development, as the IPP and SND continue to feedback on the child’s developing nervous system. Thus, early detection leading to early intervention reduces the cumulative effects of SND, consequently keeping the child closer to the path of typical development, in comparison to those who do not receive such intervention (see Figure 1).

[FIGURE 1 HERE]
Early detection and diagnosis also means that the delays and the resulting distress that families often face when trying to obtain a diagnosis for their child are avoided or minimised\textsuperscript{58}. Indeed, the main factor associated with parental satisfaction in the diagnostic process is early diagnosis\textsuperscript{41}. Thus, it is no surprise that parents want to be told at the earliest possible opportunity if there is any concern about their child’s development or well-being\textsuperscript{80}.

**SCREENING STUDIES**

The increasing knowledge of the early signs of ASDs coupled with the benefits of early intervention has led researchers to develop screening tools to identify ASDs in infancy and toddlerhood. While the majority of these studies are based on Level 2 screening (i.e., screening for ASDs in populations with developmental anomalies), some studies have attempted to identify children with an ASD who have not previously been identified with developmental problems. Prospective screening studies conducted in the general population are known as Level 1 screening studies\textsuperscript{81, 82}. Prospective studies have also been conducted with siblings of children with an ASD (ASD-sibs), as they are at increased (genetic) risk of developing an ASD\textsuperscript{83-85}.

**Delayed population (Level 2) screening studies**

Level 2 screens focus specifically on differentiating children at risk for an ASD from other developmental difficulties, such as general developmental or language delays, and are more detailed than Level 1 (or general population based) screens. They are usually administered in specialised settings, take more time to administer\textsuperscript{81, 82}, and have thus provided substantial information about ASDs in infancy and toddlerhood.

The Screening Tool for Autism in Two-Years-Olds\textsuperscript{86} (STAT) was designed to differentiate 2-year-old children at risk of AD from those at risk of other developmental disabilities. It is an interaction-based measure of 12 items assessing play, motor imitation,
communication, and JA skills. In order to develop a scoring algorithm that would maximise identification of AD, and also to examine the validity of the STAT, Stone et al.\textsuperscript{87} used this tool with 19 children with AD and 54 children with non-AD developmental disorders. The development analyses resulted in a sensitivity of 1.00, and a specificity of .91, and the validity analyses resulted in a sensitivity of .83 and a specificity of .86.

In order to develop cut-off scores for the STAT, Stone et al.\textsuperscript{88} used signal detection procedures with developmentally matched groups of 26 children with AD and 26 children with non-ASD disorders. The specificity, sensitivity, positive and negative predictive values were all very high, and the inter-rater agreements and test-retest reliability were also high. However, despite the excellent psychometric properties of the STAT, it is designed for use with children aged 2- to 3-years, and is only aimed at differentiating AD (rather than all ASDs) from other developmental disorders\textsuperscript{89}.

To determine the utility of the STAT with children below 24-months of age, and its ability to distinguish between the milder forms of ASDs and other developmental problems, Stone et al.\textsuperscript{90} administered it to 71 high-risk children (59 ASD-sibs and 12 referred due to developmental concerns) aged 12- to 23-months. Using an increased cut off score to reflect less developed social and communication skills in younger children, the screening properties for identifying children with an ASD at 14-months and older were good (sensitivity: .93; specificity: .83; Positive Predictive Value (PPV): .68; Negative Predictive Value (NPV): .97), but inadequate for 12- to 13-month olds. As the sample size of the children who went on to receive a diagnosis of an ASD was small ($n = 19$), these results should be interpreted with caution until they are replicated in larger samples.
A new tool, the Autism Detection in Early Childhood\textsuperscript{91} (ADEC), has recently been developed in Australia. Previously known as the Flinders Observational Schedule of Pre-Verbal Autistic Characteristics\textsuperscript{92} (FOSPAC), it is a semi-structured observational scale for identifying the primary core deficits seen in pre-verbal infants with AD. It has been developed as a screening tool for non-clinicians as well as professionals, and can be used with children as young as 12-months. The behaviours targeted are early social and communication behaviours.

The psychometric properties of the ADEC were assessed in a sample of 149 children with AD, 60 TD children, and 60 children with language or other developmental disorders (Young et al., 2003, as cited in Young et al.\textsuperscript{91}). It was shown to have good internal consistency (Cronbach’s \(\alpha = .85\)), good test-retest reliability \((r = .82)\), and very high inter-rater reliability \((r = .97)\). The specificity of the ADEC was .80, and the sensitivity was .70, with these figures increasing to .90 and .88, respectively, when only children less than 30-months of age were considered. However, despite the promising psychometric properties of the ADEC, these data are preliminary, and are yet to be published in a peer reviewed journal. Furthermore, these data are based on children with AD, many of whom were older than the targeted age. Thus, the properties of the ADEC for use with young children with all forms of ASD are yet to be established. Moreover, the study needs to be replicated with a younger, community-based sample.

**Prospective studies**

Prospective studies of ASDs, conducted in community-based samples, are highly desirable for a number of reasons. First, the researcher can attempt to elicit the behaviours of interest at a particular age and under standardised conditions, allowing comparison between different groups and at different time points in the child’s life. Furthermore, behaviours can be studied longitudinally, so that the relationship between early deficits and later behavioural
manifestations can be examined. In addition, prospective studies have the added benefit of not only informing us of the signs of ASDs in infancy (as do Level 2 screens), but also of being able to identify previously unrecognised cases of ASDs. Prospective studies have been conducted on both high-risk populations (ASD-sibs), and in the general population.

Sibling studies. Twin studies indicate that there is a 60–92% concordance rate for ASDs in monozygotic twins and a 0–10% concordance rate in dizygotic (DZ) twins and siblings of affected individuals. Consequently, studies of ASD-sibs have been an invaluable source of information on the very early development of ASDs. The Autism Observation Scale for Infants (AOSI) was developed to investigate the behavioural manifestations of ASDs between 6- to 18-months in a sample of ASD-sibs. It includes 18 specific risk markers for ASDs, and uses a standardised procedure for detecting each of these markers through a semi-structured, play based assessment. Using the AOSI, Zwaigenbaum et al. conducted a longitudinal study of 150 ASD-sibs (‘high-risk’ for ASDs) and 75 ‘low-risk’ infants matched on gender, birth-order, and age. Observations at 6-months of age did not predict classification of an ASD at 24-months. However, by 12-months, the presence of seven risk markers prospectively identified six of the seven children diagnosed with an ASD at 24-months, compared to two of the 58 non-ASD siblings, and none of the 23 low-risk controls. Thus, the sensitivity and specificity of the AOSI were .84 and .98 respectively.

The individual markers on the AOSI that predicted a diagnosis of an ASD at 24-months were: abnormal eye contact, visual tracking, disengagement of visual attention, orienting to name, imitation, social smiling, reactivity, social interest, and sensory-orienting behaviours (all $p < .003$, adjusting for multiple comparisons). These preliminary data now need to be replicated in the full sample. Unfortunately, as there was no non-ASD developmentally delayed comparison
group, we cannot be sure if these behavioural markers are specific to ASDs or whether they share these markers with other developmentally disabled groups of infants\textsuperscript{32}.

Bryson et al.\textsuperscript{94} prospectively followed nine of the ASD-sibs from the Zwaigenbaum et al. study\textsuperscript{32} who received an ASD diagnosis (at 24-months) at 6-monthly intervals until 24-months of age, and then again at 36-months. All of these children showed, in varying degrees, a combination of impaired social-communicative development. Furthermore, there was evidence for the emergence of two subgroups, with the first subgroup defined by a major drop in cognitive development from 12- to 24-months; the second subgroup maintained their cognitive profile of average or near average IQ. The cognitive profiles of these two groups were indistinguishable at 12-months (eight of the nine infants had average or close to average IQs), yet six of these children had severe cognitive impairments by 24- and/or 36-months of age.

Landa and Garrett-Mayer\textsuperscript{95} compared a group of ASD-sibs ($n = 60$) and TD infants ($n = 27$) at 6-, 14-, and 24-months, on their performance on each of the subscales of the Mullen Scales of Early Learning\textsuperscript{96} (MSEL; Fine and Gross Motor, Visual Reception, and Receptive and Expressive Language). As with Zwaigenbaum et al.\textsuperscript{32} and Bryson et al.\textsuperscript{94}, there were no statistical differences in the behavioural presentations of ASD and non-ASD groups at age 6-months, and there was ‘developmental worsening’ between 14- and 24-months for the ASD group. This period of slowed development between 14- and 24-months emphasises the importance of early intervention, as this increase in developmental delay may be minimised if intervention begins before this stage.

Sullivan et al.\textsuperscript{97} conducted a prospective study on response to JA (RJA) with 51 ASD-sibs at 14- and 24-months of age, and again at 30- to 36-months of age. Three groups were established: ASD ($n = 16$), ‘broader autism phenotype’ (BAP; $n = 8$), which comprised children
who displayed language and/or social delays but were not given a classification of an ASD at 3-years, and non-BAP \( (n = 27) \), which included children who did not meet classification of BAP or an ASD at 3-years. Deficits in RJA were present by 14-months in the children later diagnosed with an ASD and BAP. However, while there were large improvements in RJA for the BAP and non-BAP groups at 24-months, there was minimal improvement for the ASD group. Moreover, as performance on RJA at 14-months predicted later language and ASD outcome, Sullivan et al. concluded that RJA is an important behaviour for the early screening of ASDs, and subsequent intervention.

Another prospective study investigating the broader autism phenotype was conducted by Cassel et al.\(^98\). In comparison to non-ASD siblings \( (n = 19) \), ASD-sibs \( (n = 12) \) were found to engage in lower rates of higher-level behavioural requests (i.e., pointing at, or giving the examiner a desired toy, with or without eye contact) at 12-months, lower rates of initiating JA (i.e., pointing at an object or event out of interest, with or without eye contact; holding up a toy to show it to the examiner) at 15-months, and lower rates of RJA (i.e., following the examiner’s gaze or point) at 18-months. Although the diagnostic status of these infants has not yet been determined, the results demonstrate the broader autism phenotype in both ASD-sibs who do not go on to receive a diagnosis of an ASD, and those who do.

Mitchell et al.\(^99\), in their prospective study of 97 ASD-sibs and 49 low risk controls, found that the children who received a diagnosis of an ASD at 24-months \( (n = 18) \) showed deficits in language and communication as early as 12-months of age. These infants understood fewer phrases and produced fewer gestures by 12-months (e.g., giving, pointing, showing, shaking and nodding head, holding arms up to be lifted, and knowledge of appropriate use of real and toy objects); at 18-months, they showed delays in their understanding of phrases and single
words, use of gestures, and production of single words. As production and comprehension of words did not differ significantly between children with and without an ASD until 18-months, the authors argue that use of gestures may be more important in prospectively identifying ASDs in children less than 18-months of age.

In addition to the social and communication impairments that are consistently reported in infants with ASDs, behavioural reactivity, difficulties with transitions, and impaired motor control have also been found to account for unique variance in ASD risk in a sample of 115 18-month-old ASD-sibs\textsuperscript{100}. Furthermore, Ozonoff et al.\textsuperscript{101} found that 12-month-old ASD-sibs engaged in significantly more spinning, rotating, and unusual visual exploration of objects than the non-ASD-sibs. Thus, although social and communication impairments have been found to be the best predictors of ASDs in infancy, future research should focus on the subtle and very early behavioural manifestations alongside social and communication impairments.

Despite the recent surge of research with ASD-sibs, and the invaluable insights gained into their early development, some caution needs to be exercised when interpreting the results from these studies. Firstly, many are designed to compare groups based on risk status and not on eventual diagnosis. If the ultimate aim in these prospective studies is to improve knowledge of the early signs of ASDs in infancy, and to use these signs to prospectively identify young children, then eventual diagnostic status of these ASD-sibs becomes critical\textsuperscript{102}. Secondly, high-risk samples are unique and are not representative of a ‘true’ prospective sample. Children who have grown up in an environment already affected by an ASD may have different symptomology in comparison to those children with an ASD who were not reared in that environment. Moreover, it has been found that children with an ASD from multiplex families are higher functioning in adaptive skills and cognitive development than those from singleton families\textsuperscript{103}. 

Thus, numerous factors need to be considered as possible influences contributing to differences in development, including alteration in parent-child interaction, early recognition of symptoms and subsequent intervention, affected parenting styles due to exposure to early intervention techniques, and parental stress\textsuperscript{102}. In addition, genetic expression of ASDs may differ in multiplex compared to singleton families, although there is little research to date investigating this possibility.

**General population (Level 1) screening studies.** Level 1 ASD screens are used to identify children for general developmental disability, with specific emphasis on the signs of ASDs. These screens are used in the general population, and are usually applied in community health services, such as in infant and child health centres or in general medical practice settings\textsuperscript{81, 82}. There are currently very few screening studies for ASDs that have been conducted in community-based settings, and all of these have used tools that screen for ASDs at only one specific age.

Baron-Cohen and colleagues conducted the first prospective study of ASDs. They developed the Checklist for Autism in Toddlers (CHAT)\textsuperscript{38}, designed to be administered in a primary health care setting to identify 18-month-old children at risk for an ASD. This brief observational tool was initially administered to 41 ASD-sibs and 50 TD children, all aged 18-months. Three key items (protodeclarative pointing, gaze monitoring, pretend play) were successful in identifying children who later received an ASD diagnosis at 36-months. Baron-Cohen et al.\textsuperscript{104} subsequently used the CHAT on 16,235 18-month-olds during their routine developmental check-up. Twelve children were identified as ‘at risk’, with 10 of these children receiving a diagnosis of an ASD, and two receiving a diagnosis of DD; these diagnoses remained stable at 3.5-years, giving a false positive rate of 16.6%. In a long-term follow-up study of this
same population, Baird et al.\textsuperscript{105} found that although the CHAT had excellent specificity (.98), it lacked sensitivity (.38), as 50 additional children were identified at age 7 as having an ASD, none of whom had been identified as at risk at 18-months. The low sensitivity of the CHAT reduces its use as a screening instrument, as a large percentage of children with an ASD (around 60\%) will not be identified by the CHAT at 18-months.

A modified version of the CHAT was developed in an attempt to increase the sensitivity of the tool. The M-CHAT\textsuperscript{106} relies entirely on parental report and is designed for use with 24-month-olds; unlike the CHAT, it has a lower threshold for identifying ASDs. A non-selected population of 1,122 18- to 25-month-olds and a high-risk sample (referred from early intervention services) of 171 18- to 30-month-olds were screened using the M-CHAT. Six items in the areas of social relatedness and communication were found to best discriminate between children diagnosed with and without an ASD (protodeclarative pointing, response to name, interest in peers, bringing things to show parents, following a point, imitation). Using various cut-off scores on the checklist, sensitivity ranged from .87 – .97, specificity ranged from .95 – .99, and PPV ranged from .36 – .80, depending on which cut-off scores were used, and whether the M-CHAT was followed-up with a scripted telephone interview. These preliminary data suggest that the M-CHAT is able to discriminate between ASDs and other DDs by 24-months, and has a higher sensitivity for detecting ASDs than the CHAT.

In a study by Ventola et al.\textsuperscript{107}, 195 children (mean age: 24-months) who failed the M-CHAT were grouped into DD ($n = 15$), Developmental and Language Disorder (DLD; $n = 30$), and ASD ($n = 150$) to investigate differences in symptom presentation. Once overall language level was controlled for, only four items significantly differed between the DD/DLD and ASD groups. These were all JA and social responsiveness items (response to name, pointing for
interest and to request, ability to follow a point), reinforcing past literature that social responsiveness and JA behaviours are core, and particularly unique, deficits in ASDs.

In order to address the usefulness of the M-CHAT as a screen for ASDs in a community-based sample, as well as to establish absolute sensitivity and specificity, Kleinman et al.\textsuperscript{108} screened 3,309 low-risk children (new cases) as part of their well-child care visits, and a further 484 high-risk children referred for early intervention. All children were screened at 16- to 30-months (Time 1), and followed-up at 42- to 54-months (Time 2). For the total sample, PPV at Time 1 was close to that of the original study (.36 – .74), again depending on whether a follow-up phone interview was used; PPV for the total sample at Time 2 was similar (.59 – .74). However, for the low-risk sample, PPV at Time 1 was extremely low (.11 ± .05) when the M-CHAT was used alone. When used in conjunction with a follow-up phone interview, it increased to .65 ± .17. Thus, the PPV increases to an acceptable level, but only in conjunction with a follow-up phone interview, which is consistent with the findings of both Pandey et al.\textsuperscript{109} and Robins\textsuperscript{110}. These data suggest that the use of the M-CHAT alone as a screen for ASDs in a community-based sample is problematic. The M-CHAT may be useful in identifying children in need of further assessments, but should not be used as a screen to exclude the possibility of an ASD\textsuperscript{111}.

The Q-CHAT\textsuperscript{112}, a quantitative version of the CHAT, marks a major revision of the instrument. Like the M-CHAT, it relies solely on parental report, and contains 25-items rated on a 5-point likert scale. Its test properties and clinical validity have not yet been established, although preliminary data on a sample of 779 children (unselected group: mean age 21-months; ASD group: mean age 44-months) has resulted in a range of scores that approximate a normal distribution. Thus, the Q-CHAT may be a useful instrument to measure trait differences in the
general population, and not just in the ASD population. However, its revision into a parental report only measure lends itself to the problems associated with these types of measures, as discussed previously.

An ongoing longitudinal, prospective study, called the FIRST WORDS® project, uses the Communication and Symbolic Behaviours Scales (CSBS) as a screen with children in the general population, recruited from health and childcare clinics. The CSBS comprises an Infant-Toddler Checklist (ITC) that parents complete when their child is below 24-months of age, and a Behaviour Sample, which is a direct evaluation of the child after 18-months of age by a clinician, which is videotaped for later analysis. Wetherby et al. examined the social and communication behaviours of 123 children (50 with an ASD, 23 with DD, and 50 TD children) aged 18- to 26-months using the CSBS who were recruited from the FIRST WORDS® project. Compared to children with DD, who were matched on age and developmental level, the children with an ASD were found to display five core social and communication deficits. These included deficits in gaze shifts, following of gaze/points, rate of communicating, acts for joint attention, and inventory of conventional gestures.

In order to determine the efficacy of the ITC as a general population screening tool, 5385 children from the general population were administered this checklist between 6- to 24-months of age. Of the 60 children who went on to receive an ASD diagnosis, 53 (93%) screened positive between 9- to 24-months. However, although the sensitivity of the ITC between 9- to 24-months is excellent, it is unable to distinguish between children with an ASD and those with communication delays, as 813 children were identified on the ITC as needing further developmental surveillance.
A review of ASDs in infancy and toddlerhood

Only one other community-based ASD screening study has been conducted to date. Swinkels et al.\textsuperscript{117} developed an instrument known as the Early Screening of Autistic Traits Questionnaire (ESAT). A population of 31,724 children aged 14- to 15- months were first pre-screened at well-baby clinics using a 4-item screening instrument, and screen positive infants were then evaluated using the 14-item ESAT. Eighteen children were found to have an ASD, indicating that it is possible to identify unrecognised cases of ASDs as early as 14-months. The items that were most predictive of ASDs were, once again, social-communicative in nature. ‘Stereotypical movements’ was least predictive, reinforcing the earlier suggestion that social-communicative behaviours are the strongest predictors of ASDs, and repetitive behaviours (or stereotypies) are, perhaps, more indicative of general intellectual disability\textsuperscript{23,118}.

The use of the ESAT as a general population screen in its current form would be problematic, as it was found to have a large number of false positives (42 in total); however, none of these were TD children. Although the authors could not determine overall sensitivity, they indicated that it would have been low as their number of identified cases of ASDs was low in comparison to current prevalence rates\textsuperscript{119}.

**DIAGNOSING ASDs IN TODDLERS: INSTRUMENTS AND STABILITY OF DIAGNOSIS**

The findings from the screening studies reviewed above indicate that it is possible to identify ASDs in infancy and toddlerhood. It has also been shown that it is possible to accurately diagnose ASDs as early as 2-years of age with instruments such as the ADI-R\textsuperscript{120}, a standardised, semi-structured parental interview, and the ADOS\textsuperscript{121,122}, an observational instrument consisting of four modules devised for individuals with varying language abilities. However, it has been found that that ADOS sometimes has lower specificity and sensitivity for classification between
AD and other ASDs\textsuperscript{123-125}. Recently, Gotham et al.\textsuperscript{125} attempted to improve the sensitivity and specificity of the ADOS in differentiating the various ASDs, by altering the current algorithm. A 12-31\% increase in specificity in differentiating between the ASDs was achieved with non-verbal children. Furthermore, a replication study by Gotham et al.\textsuperscript{126} found that the sensitivity and specificity of these revised algorithms approximated or exceeded those of the original algorithms (except for young children with PDD-NOS and phrase speech). These revised algorithms are yet to replace the current algorithms, as these findings await further replication with other research samples.

Although the ADOS is the best available instrument for diagnosing ASDs in children as young as 2-years, its use with children younger than 2 is limited. A toddler version was therefore developed by Luyster et al.\textsuperscript{127}, with an algorithm developed for all children aged 12- to 20-months and non-verbal children aged 21- to 30-months, and another for verbal children aged 21- to 30-months. The data on 272 children aged 12- to 30-months of age produced excellent specificity and sensitivity values of 93\% to 95\%. Due to the variability in early development, the authors propose that the scores on the new algorithms should be used to indicate ranges of concern (i.e., little, moderate, significant concern), rather than using traditional ‘cut-off’ scores. The data await replication with a larger sample, and data on the stability of diagnosis using the toddler version are not yet available.

Given there are some problems associated with the ADOS in correctly differentiating the ASDs, and with the ADI-R in correctly diagnosing AD in children with mental ages below 18-months\textsuperscript{128-130}, it has been suggested that the two instruments be used together\textsuperscript{124}. Le Couteur et al.\textsuperscript{131} found good agreement between the instruments in a preschool sample aged 24- to 49-months, especially for those with ‘classic autism’ (AD). However, Ventola et al.\textsuperscript{132} found poor
agreement with the ADOS and ADI-R in young children as they did not display enough repetitive behaviours and stereotyped interests to meet the cut-off for AD on the ADI-R. Therefore, Wiggins and Robins\textsuperscript{133} excluded the behaviour domain on the ADI-R when assessing toddlers at risk for an ASD, and found a significant improvement in agreement between the ADI-R and other measures (including the ADOS). These findings indicate that it is advisable to use the ADI-R together with the ADOS, in conjunction with clinical judgment, when diagnosing very young children.

**Reliability of diagnosis at age 2**

Diagnoses of ASDs at around 2-years of age have been found to be accurate and stable over time\textsuperscript{134}. Lord\textsuperscript{49}, using clinical judgement, found that 27 children out of 30 retained their diagnostic classification of an ASD from 2- to 3-years of age. Eaves and Ho\textsuperscript{135} found that 79\% of children given a diagnosis of an ASD at age 2½-years retained their diagnosis at age 4½-years. However, the stability of diagnoses for ASDs other than AD was not as stable across time. Turner et al.\textsuperscript{136} examined the developmental outcomes of 2-year-old children 7 years after they received a diagnosis of an ASD. It was found that 88\% of the children who received an ASD diagnosis at age 2-years received the same diagnosis at 9-years of age. In their study of 77 children aged 16- to 35-months, Kleinman et al.\textsuperscript{137} reported that 80\% remained in the same diagnostic category at 42- to 82-months of age. As with previous studies, a diagnosis of AD was more stable than that of a PDD-NOS diagnosis (85\% versus 47\%).

Charman et al.\textsuperscript{138}, also investigating the outcome of children 7 years after their initial diagnosis at 2-years of age, found that 22 of the 26 children diagnosed with an ASD at 2-years (based on clinical judgement) continued to meet this diagnosis at 9-years of age. However, their findings on the stability of diagnosis based on psychometric and standardised tests, as opposed to
clinical judgement, were not as clear, with children crossing diagnostic boundaries as they aged. Charman et al. concluded that the assessment of early social-communication behaviours (using, for example, the ADOS) gives a better indication of the diagnostic profile of young, non-verbal children than standard psychometric tests measuring IQ and language abilities.

In summary, the follow-up studies reviewed above indicate that the diagnosis of ASDs is reliable in children aged 2-years. However, it is imperative that the diagnostician has sufficient training and experience in the assessment and diagnosis of ASDs, and utilises appropriate tools for young, non-verbal children, which are used in combination with clinical judgement.

**SUMMARY AND FUTURE DIRECTIONS**

The prevalent finding from studies on ASDs in infancy and toddlerhood is that abnormalities in social attention and communication behaviours are evident from the first year of life, and are the most predictive early signs of an ASD diagnosis. In the area of social attention, these markers include a lack of eye contact, social interaction, social smiling, imitation, orienting to name call, appropriate facial expressions, and interest and pleasure in others. In the area of communication, these markers include a lack of vocal communication, JA skills (protodeclarative pointing, following a point, gaze monitoring, referencing objects/events), showing and requesting behaviours, and gestures. Impairments in imagination skills, such as the use of pretend play, have also been found to be important markers in late infancy/toddlerhood.

Although sensory/motor behaviours and stereotypies are seen in some infants with an ASD, these behaviours may be more indicative of general intellectual disability, and these behaviours may not become apparent until at least 3-years of age in some children. Currently, they may not serve as important predictors of ASDs in infancy.
Level 1 screening instruments, using social attention and communication behaviours as key items, have been able to prospectively identify previously unidentified cases of ASDs in community-based samples. A highly predictive, but brief, observational tool containing a checklist of the behaviours that are absent in infants with an ASD would prove invaluable for the detection of these infants, as children that would previously go unrecognised could be identified though routine developmental monitoring, and reliably diagnosed at 2-years of age. This is important, as only 50% of parents of children with an ASD suspect a problem before 12-months\textsuperscript{13}. However, it is apparent from the studies reviewed here that, as acknowledged by Charman\textsuperscript{139} (p1), there are currently no instruments available with adequate sensitivity and specificity to recommend universal screening. Therefore, there remains a need for more prospective studies of infants conducted in community-based settings, as the few conducted to date have reported poor sensitivity on the measures used, or have high false positive rates.

The routine and repeated monitoring of behaviours throughout the infancy period, rather than a single screening at a given age, may prove more useful in detecting ASDs in infancy. The prospective community-based studies reviewed here all utilised a screening tool at a single given age. In contrast to this approach, the \textit{repeated} monitoring of infant development will serve to increase the chances of identifying early manifestations of ASDs, consequently increasing the sensitivity of the screening tool utilised. In addition, repeated sampling will help to track the subtle changes that occur in infants with an ASD overtime\textsuperscript{140}, and aid investigation into what seems to be a critical period between 12- and 24-months of age, where a subset of children with an ASD progressively lose cognitive skills, while another maintains cognitive abilities\textsuperscript{94,95}. Furthermore, the phenomenon of regression is well known to occur during this time period. Thus, future prospective studies should focus on systematically investigating not only the
behavioural changes that occur during this important developmental period, but also the
milestones that children with an ASD reach in relation to those reached by their TD peers. In
addition to aiding early identification, such a focus on the early development of the ASD
phenotype will ultimately contribute to understanding the underlying neuropathology leading to
the cognitive and behavioural deficits in ASDs.
REFERENCES


A review of ASDs in infancy and toddlerhood


|---|---|
A review of ASDs in infancy and toddlerhood


106. Robins DL, Fein D, Barton ML, Green JA. The Modified Checklist for Autism in Toddlers: An initial study investigating the early detection of autism and pervasive


FIGURE LEGEND

_Figure 1._ Mundy and Crowson’s (1997) cybernetic model of ASDs.
FOOTNOTES

ª Unless otherwise stated, ASD will be used throughout the review to refer to Autistic Disorder, Asperger’s Disorder, and Pervasive Developmental Disorder – Not Otherwise Specified.
ACKNOWLEDGEMENTS

The first author was supported by a Sir Robert Menzies Memorial Foundation Allied Health Scholarship during the writing of this paper. We would also like to thank Izabela Fedyszyn and Pat Monteleone for providing feedback on earlier drafts of this manuscript.