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Developmental approaches to understanding and treating autism

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ABSTRACT

Over the past decade our understanding of early social communication development in young children with autism has undergone a remarkable change. We now know something about how young children with autism process the social world in a very different way from typical children. This has led to truly *developmental* models of autism. In turn, these have had profound impacts on research and practice. Several screening instruments to prospectively identify autism have been developed. In some cases autism can be diagnosed in children as young as 2 years of age. The study of ‘high risk’ siblings has allowed prospective study of infants from as young as 6 months of age. There is increasing evidence that intervention approaches that focus on social and communication development can ameliorate symptoms and changing the developmental course of the disorder. This article will highlight some of the key theoretical and clinical lessons learned from this decade of research.

Keywords: autism, autism spectrum disorder, screening, diagnosis, intervention

Autism emerges early; autism research with infants and toddlers arrives late

Over the past decade there has been remarkable progress in our understanding of the early development of children with autism spectrum disorders (ASDs). Until the 1990s it was rare for children to receive a diagnosis of autism until the age of 3 or 4 years. Therefore, much of the historical literature in both the clinical and research fields starts with descriptions of children with autism at age 4 to 5 years or even older. This is despite the fact that in most cases autism has an onset in infancy [1], and is the result of genetic and other organic aetiological factors that affect brain development very early in life [2]. However, progress has recently been made in the earlier identification of children with ASD [3,4,5] and many children are now first identified in the pre-school period [6,7].

Whilst both psychiatric classification systems state that, at least to meet criteria for the ‘core’ disorder of childhood autism [8] or autistic disorder [9], symptoms of autism are required to be present in the first 3 years of life, as evidenced by abnormalities in social interaction, language as used in social communication and early play skills, until the 1990s few studies had been conducted with samples under the age of three years. This is not to challenge the notion that in many if not most cases of autism spectrum disorder, excepting perhaps those with very high IQ or those who meet criteria for Asperger syndrome, there is some developmental anomaly within the first three years. Indeed, some recent evidence suggests that at least in the case of childhood autism some early developmental perturbation that only in some but not all cases meets recognized criteria for regression might occur for the majority as opposed to the minority of cases [10,11,12]. It may well be that parents do not always notice or pick up on more subtle changes in their children’s social and communicative development from infancy to toddlerhood unless there is frank regression, most

typically evidenced in a loss of expressive language skills but also in preverbal social communication skills. Rather, it is to point out that apart from rare exceptions [13] until the mid 1990s the majority of information above developmental from toddlerhood through the preschool years came from retrospectively-reported information from parents. The growth in our knowledge base regarding the presentation of autism in the preschool over the past decade is demonstrated by a simple experiment. In December 2009 entering the search terms ‘autism’ and ‘toddlers’ into PudMed identified 114 articles: 103 of these were published *after* 2000; 83 of which were dated from 2005.

Several factors have driven this change, including efforts to improve earlier identification with the recognition that earlier-delivered intervention may improve outcomes and prevent ‘secondary’ neurodevelopmental disturbances [14,15]; the development of prospective screening instruments to identify possible cases of autism from the first few years of life [16,17]; and the use of the genetic ‘high-risk’ research design of prospectively studying younger siblings of children with a diagnosis of autism from the first year of life [18,19,20]. This decade of work has uncovered important evidence regarding the developmental trajectory of autism spectrum disorder from infancy and toddlerhood, through the preschool years into school age and beyond.

Whilst many of the insights gained from these clinical and experimental studies have proved clinically useful they have also raised considerable challenges. For example, early diagnosis raises questions about at what age autism can be diagnosed reliably and how stable the diagnosis is over the course of the preschool years, as well as the ability to predict (at least at a group level) outcomes many years later. Screening for a developmental disorder raises clinical issues for parents and

professionals, including those relating to the concept of ‘risk status’, certainty of diagnosis, advice about management and the availability of appropriate services. Another notable challenge is the substantial variability in early development trajectory in children with autism and our difficulty in disentangling the extent to which these variable trajectories for individual children are due to intrinsic versus extrinsic factors. The challenge for the next decade is to improve the evidence-base for social communication and behavioural interventions that may lessen the impact of the disorder and improves outcomes for children and their families.

Novel methods to study the earliest emergence of autism

Twenty years ago studies began to report on early social and communication behaviour by analysing information from early home movies shot before the child later went on to receive a diagnosis [21,22]. Many groups have now used this method and the data suggest that home videos of infants who later on develop ASDs reveal that these infants already manifest difficulties and impairments in communication, social relationships and sensory motor development. In the very earliest time period studied (the first 6 months of life), dyadic and intersubjective abnormalities have been detected, as well as reduced amounts of time paid to social stimuli. By the end of the first year of life a wide range of triadic early social-communicative differences are apparent (at least at a group level): reduced orienting to name; impoverished joint attention behaviours; some early motor abnormalities and reduced emotional expression (see [19]; for a review). These early symptoms were usually most clearly identified during the second year of life, although some studies identified abnormalities around the child’s first birthday. This methodology has some advantages in that natural occurring behaviour prior to diagnosis is evaluated. However, home movies also suffer from limitations as the data is not standardized and

parents may chose to videotape their children when the children are at their best, for example not necessarily while manifesting some of the behaviours which may be early signs of autism.

Over the past decade a number of groups worldwide have initiated truly prospective observational studies by exploiting the relatively high recurrence rate of autism in families [18,20]. This allows the possibility to recruit a cohort of younger siblings of an older child with an autism diagnosis and to follow their development over time; with the likelihood that a proportion of the cohort will go on to develop autism. This is by nature a long-term undertaking since reliable diagnosis cannot be established much before the age of three years. However, the design also allows one to test differences between the ‘high risk’ sibling group and low risk controls with no family history of autism; which some groups have called a ‘broader autism phenotype (BAP) analysis’. These studies have found a number of differences, again mostly in early social communication behaviours and mostly emerging around the younger siblings’ first birthday. In addition to behavioural studies, several groups have also begun to use experimental brain imaging measures, such as evoked response potentials (ERPs), to test if there may be disrupted neural processing of both social and non-social stimuli in high risk siblings [23,24].

To date, only four groups have reported on associations among early development during the first year or two of life and later diagnoses of ASDs. Zwaigenbaum and colleagues [25] examined the development of high risk and low risk infants from 6 to 24 months and identified several behavioural markers at 12 months that predicted later diagnoses of ASD, including atypical eye contact, visual tracking, disengagement of visual attention, orienting to name, imitation, social smiling, reactivity, social interest, and sensory-oriented behaviours. From the same

group, Mitchell and colleagues [26] added that siblings diagnosed with ASD at 24 months in this sample had delays in gestural communication (i.e., giving, pointing, gestures) as reported by their parents at 12 months.

Landa and Garrett [27] found that on the Mullen Scales of Early Learning (MSEL [28]) the group with the ASD outcome had the slowest developmental trajectory, with a significant decrease in development between 14 and 24 months. Landa, Holman and Garrett-Mayer [10] found that siblings who received an early ASD diagnosis (at 14 months) showed diminished communication and play behaviour at age 14 months but that those who only received a diagnosis at the later 24 month assessment, some skills continued to grow but at a slow rate between the two time points, others plateaued, whilst others (shared positive affect and gestures) decreased.

The study by Ozonoff and colleagues [11] was the first to report on a sample as large as 25 siblings who went on to receive an autism spectrum (ASD) diagnosis at 36 months. They compare rates of three early social communication behaviours (gaze to faces, social smiles and directed vocalizations) captured by observers during assessment sessions when the siblings were 6, 12, 18, 24 and 36 months of age. They found a *slowing* of development in terms of raw scores on the general developmental assessment (MSEL); that is, the high risk siblings begin to fall behind the low risk controls. In contrast there was an actual *decline* in the rates of the early social communication behaviours i.e. an actual reduction in frequency of social responses. This loss began around the first birthday and continued across the second year of life, and on some measures into the third year. This pattern of loss of skills was found in over three-quarters of the high risk group. However, at age 6 months there were no differences between the groups; indicating that the high risk siblings who went on to meet diagnostic criteria for ASD at 36 months of age showed the same rates of early

social communication behaviours as controls. The second notable, and perhaps surprising, finding was that by parental report looking back from the timepoint of the 36 month interview loss of skills was reported for only a minority of those children whose social communication skills declined over the second year of life (at least when interacting in an unfamiliar setting, with an unfamiliar adult in the observations taken in the lab). This is surprising in part because families taking part in these ‘high risk’ sibling studies understand the familial nature of the design and we might expect worried parents to be hypervigilant for early signs that something is not right with their younger child.

We have always known that regression or loss of skills is present by (retrospective) parental report in some 15% to 30% of cases; depending on the definition employed and the sample [29]. Ozonoff and colleagues [11] suggest that regression might be the norm and not the exception in autism. A similar suggestion was recently made by Pickles and colleagues [12], albeit based on retrospective parental report. They found not only that regression was very specific to autism, as it was almost never found in children with language impairment without autism, but also a strong association between age of first words and likelihood of undergoing regression. That is, frank loss of language skills was associated with switching from the most advanced early language to being amongst the slowest (in terms of eventual onset of phrase speech). We do not know what the nature and causes are of the neurodevelopmental perturbations that underlie regression but the existence of such ‘high risk’ prospective studies offers an opportunity to investigate these questions.

Prospective screening studies to identify autism in infants

At the beginning of the 1990s, Simon Baron-Cohen and colleagues set out to develop a specific screen for autism. Drawing on evidence that impairments in social

orienting behaviours (including joint attention) and pretend play differentiated preschool children with ASD from children with general developmental delay [30,31,32], a new instrument was developed. The CHAT (CHecklist for Autism in Toddlers) was designed to prospectively identify autism at 18 months of age. This age was chosen as an appropriate screen "window" [33] because joint attention and pretend play typically emerge at this time in normal development. The CHAT assesses simple pretend play (appropriate use of a teaset, doll play, object substitution) and joint attention behaviours (pointing for interest – in combination with eye contact – and following gaze) by parental report and health practitioner observation through direct testing.

The first study tested the effectiveness of the CHAT as a screening instrument in a genetic 'high-risk' sample of forty-one 18-month-old siblings of children already diagnosed with autism with ASD [34]. Whilst none of 50 unselected 18 month olds failed all 5 key items, four of the children in the high-risk group did so. A year later, when the children were 30 months old, a follow-up was carried out. None of the unselected children had been diagnosed with ASD. The four children in the high-risk group who had failed the five key items were diagnosed with autism.

To test the effectiveness of the CHAT in a large general population, health visitors and general practitioners in the South Thames region of the UK used the questionnaire with 18-month-olds as part of routine health surveillance [35]. 16,235 18-month-olds were screened using the CHAT, mostly by health visitors (community nurses). We predicted that those children who at 18 months failed all five key items would be at the greatest risk for ASD. We called this the *high risk for autism group*. Children who failed both items measuring protodeclarative pointing (pointing for interest), but who were not in the high risk for autism group, were predicted to be in

the medium risk for autism group. Children who do not fit either of these profiles were predicted to be in the *low risk for autism group*. In order to minimise false positives, a two-stage screening procedure was adopted. Children who were initially screen positive (at the high or medium risk threshold) received a second administration of the screen one-month later, via a telephone follow-up.

Used in this 2-stage way, the positive predictive value of the screening instrument was high (83% for ASD using the high-risk threshold). However, sensitivity was poor (18%), indicating that four-fifths of the children subsequently identified as having ASD in the study population were missed on screening. If a one-stage screening procedure only had been adopted the proportion of children with autism identified increased to 38%, although in clinical use this would have entailed the assessment of more screen false positives. The CHAT population study demonstrated that failing a combination of joint attention and pretend play items (by both parental report and health practitioner observation, and on both administrations of the screen) indicated a significant risk for developing autism. However, although the CHAT screen had a high positive predictive value its sensitivity was moderate at best and the findings cannot support a recommendation for total population screening at a single time point [35].

However, there are differences between the use of a screen in a research study (where the criteria set for risk and onward referral is applied without clinical decision-making) and the use of a screen in routine health surveillance (where clinical decision-making about possible developmental problems is used in combination with the risk criteria to determine referral). Fortunately, there is some evidence that skilled clinical opinion can also enhance detection. This is good surveillance but not screening. Subsequent to our initial attempt to screen a population sample, we have

used the CHAT to identify children with autism at age 20 months for inclusion in an early intervention study [36]. Only the key screening items (across both the parent report and practitioner observation sections) measuring joint attention and play behaviours were included in a shortened version of the screen, again administered at 18 months. In order to minimise screen false positives, health practitioners were asked to refer children who not only failed all the key items but about whom they were also concerned about possible ASD.

The children notified as failing all pointing and pretence items by parent report, confirmed by professional observation, had a repeat CHAT by telephone within 2 weeks. Of 51 children referred to the study, 5 passed on retest by telephone (compared to 26 from 38 who passed on retest in the original population study; Baird et al., 2000). Of the remaining 46, following a diagnostic assessment, 31 had autism, 5 PDD, 6 a receptive-expressive language disorder, 2 global developmental delay, and 1 child had ADHD. Only one child had no developmental problem identified at assessment. Thus, when the score on the CHAT screen was combined with clinical judgment or concern about possible autism the positive predictive value was very high even for a one-stage (CHAT-1 only) administration (71% for all ASDs and 88% for all developmental disorders). This concurs with studies that have used the CHAT screen in referred samples [37,38,39]. However, sensitivity cannot be estimated from this study as the screen was not used on a total population that was then followed-up to identify screen false negatives.

A number of other groups have also developed and begun to test screens for ASD both in total population samples and in clinically referred samples. Robins et al. [38] developed a modified version of the CHAT (the M-CHAT) that included additional items measuring other aspects of early social communication impairments

characteristic of autism (e.g. response to name, imitation) as well as repetitive behaviours (e.g. unusual fingers mannerisms) and sensory abnormalities (e.g. oversensitivity to noise). The M-CHAT is a parent report instrument only, the health practitioner does no direct testing. In their initial report, Robins et al. [38] had tested 1,122 unselected children (initially at 18 months but subsequently at 24 months of age) and 171 children referred for early intervention services (considered to be at high risk of having an ASD or other developmental disability). The screen (initially with 30 items, subsequently reduced to 23 items) was administered by paediatricians in the unselected sample and by early intervention service providers in the referred sample. Following analysis of the first 600 returns, a cut-off was set as failing 2 from 6 'critical items' or any 3 items from the total of 23 items. Once a child failed the M-CHAT the research team re-administered the screen by telephone and if a child still scored above cut-off the family were invited for an assessment.

Of the 58 children who failed on both administrations of the M-CHAT, 39 subsequently received an ASD diagnosis and the remaining 19 were found to have language or global developmental delay. Note that only 3 of the 39 children with ASD were from the unselected population, with the majority being identified from the sample referred for early intervention services. The authors found that the items that best discriminated between children with ASD and children with other developmental problems were those that measured joint attention behaviours (pointing and following a point, bringing things to show), social relatedness (interest in other children, imitation) and communication (response to name). A recent study [37] has reported on the M-CHAT with a new sample of 3,793 children aged 16 to 30 months. Kleinman and colleagues found a positive predictive value of 0.36 for the initial screening which improved to 0.74 for the screening plus the follow-up telephone

interview. Again, most cases were identified from the 'high risk' sample of children referred for early intervention services or due to a developmental concern. Follow-up studies will be required to estimate the instrument's parameters when used on an unselected population, in particular its sensitivity in detecting cases of ASD in children about whom there had not been previous developmental concerns.

Buitelaar and colleagues in the Netherlands have developed a screening instrument (Early Screening of Autistic Traits; ESAT) to identify ASD in 14-month-old children [40,41]. Dietz et al. [41] completed screening of 31,724 children at 14 months of age. Health practitioners at a well-baby clinic appointment administered an initial screen of 4 items. If a child failed 1 or more of the 4 items (measuring varied play with toys, readability of emotional expression and sensory abnormalities) they were offered a follow-up home visit. The choice of these items was based on comparison of frequency of endorsement of items in an unselected sample of 8 to 20 month olds and retrospective parental report of how their child *would have* scored on items at 14 months of age in two older, already diagnosed samples of children with ASD and children with ADHD [40]. At this visit a longer version of the ESAT (14 items that included many social communication items such as eye contact, response to name etc.) was administered alongside other developmental assessments. Children who failed 3 or more items of the 14-item ESAT were invited for a diagnostic evaluation. The ESAT did identify children with ASD (N=18) and also children with language disorder (N=18) and intellectual disability (formerly 'mental retardation') (N=13). Once again, establishing the instrument properties, particularly the sensitivity, of the ESAT will require longer-term follow-up of the entire population sample in order to identify missed cases. Similarly to the M-CHAT analysis conducted by Robins et al. [38], the items that discriminated best between children

with and without ASD were items assessing early social communication impairments, including ‘shows interest in people’, ‘smiles directly’ and ‘reacts when spoken to’.

One notable feature of this study, in comparison with the CHAT population study, was that the rate of refusal of diagnostic appointments was considerably higher (no parents refused to attend follow-up appointments in the CHAT study). This may indicate that parents of children aged 14 months were more reluctant to accept that their child might have a developmental problem compared to at age 18 months in the CHAT study. The issues of screen accuracy (both in terms of positive predictive value and sensitivity) and parental acceptance and recognition are important considerations when considering the ‘best’ time to employ a general population screen for ASDs. An additional important factor in implementing screens is the balance between ‘false positives’ and ‘false negatives’. False positives tend to cost services; whereas false negatives tend to cost the child and parent.

Diagnostic stability of ASD diagnosis made in toddlers

One of the most significant challenges and concerns of this new era of prospectively studying children with autism spectrum disorders from the age of 2 and 3 years concerned diagnosis. Given the relative lack of experience of applying the diagnostic criteria to children of this age, even amongst the relatively expert clinical teams conducting such studies, one critical question quickly arose: Was the diagnosis accurate and stable when applied at this age? Fortunately, many research teams were studying cohorts of toddlers by the mid-1990s and evidence regarding the issues of diagnostic accuracy and stability began to emerge as the cohorts were followed up into preschool and in the mid 2000s into the school age years. What emerged from these programs of work were some clear messages (autism *can* be accurately

diagnosed in 2 year olds) but also some areas of uncertainty (in some cases diagnosis appears less stable) that will take continued study to resolve.

Table 1 summarises the diagnostic outcome studies that have followed cohorts of children from initial diagnostic assessments around the age of 2 years into the preschool years and in several of the more recent studies [42,43,44] into the school age years. The first series of studies [45,46,47,48] all showed high stability of diagnosis in particular for ‘core’ autism, with somewhat lower stability for broader autism spectrum disorder (ASD) and pervasive developmental disorder not otherwise specified (PDD-NOS). The movement across the ASD/PDD-NOS diagnostic category boundary was somewhat different in the different studies, with Stone et al. [48] finding that 4 out of 12 children who met broader ASD criteria at the initial assessment did not meet criteria for an autism spectrum disorder at follow-up, whereas Cox et al. [45] found that 7 from 31 children who did not receive an autism spectrum diagnosis at the initial assessment met criteria for broader ASD at follow-up. Several of the studies [45,46,48] concluded that, for 2 years olds, expert clinical judgement is more reliable than the standard diagnostic instruments the Autism Diagnostic Interview-Revised (ADI-R [49]) and the Autism Diagnostic Observation Schedule – Generic (ADOS-G [50]). Several studies also found that behaviours from the third symptom cluster that defines autism – restricted and repetitive behaviours and activities – were less evident at 2 years of age than at 3 to 5 years of age [41,42,43].

The samples in these studies differ in a number of characteristics, including how and for what purposes they were ascertained (e.g., prospectively using the CHAT screening instrument in the Cox et al. study vs. following clinical referral for possible autism in the Lord, Moore and Goodson and Stone et al. studies), IQ, language ability

and the different use and implementation both of standard diagnostic instruments but also of DSM-IV and ICD-10 diagnostic criteria, and these factors might account for the differences found.

 Table 1 about here

The more recent studies differ from the earlier ones in a number of features, most notably considerably larger sample sizes (N=172 [43]; N=77 [51]) and follow-up periods that extend to age 7 years in the Charman et al. [42] study and age 9 years in the Lord et al. [43] and Turner et al. [44] studies. Broadly, the lessons learned are the same – that the diagnosis of autism is highly stable in these samples but that of broader ASD/PDD is less so. Lord et al. [43] found that age 2 scores on measures of repetitive and restricted behaviours and activities predicted an autism diagnosis at age 9 years. In some of these more recent studies there was greater movement from having an ASD diagnosis at age 2 years to a non-spectrum diagnosis at age 4 [51,52]. Whilst the authors report the factors associated with these ‘good outcomes’ – mainly higher IQ and better language competency – it is important to remain cautious regarding predictors of poorer or better outcomes. However, the general pattern is of high stability of diagnosis for autism, replicating the earlier pioneering longitudinal work of Sigman and colleagues who found high stability of diagnosis of children from 4 years of age through to mid childhood (13 years) and young adulthood (19 years) [53,54].

For clinicians the lesson is to accept that autism is a *developmental* disorder and at a very young age there may be less certainty regarding the pattern of behaviour that a child is showing and the likelihood of them continuing to meet diagnostic

criteria into the future. Charman and Baird [16] discuss the importance of understanding the diagnostic process as an iterative one to be worked out between clinical teams and parents over time and that concepts such as a ‘working diagnosis’ or ‘working hypothesis’ can be helpful. However, at the same time, clinical teams need to be aware of the need to provide sufficient certainty regarding the child’s condition that they are not refused appropriate services following assessment. One other important clinical reminder is that whilst the trajectory of early emerging impairments in social and communication development accompanied by rigid and repetitive behaviours and interests characterizes many children on the autism spectrum, there is a sub-group of particularly verbal and intellectually able children who go onto to receive a diagnosis of autism (sometimes called ‘high functioning autism’) or Asperger syndrome who may not receive a diagnosis in the preschool years. There is also another group who might meet diagnostic criteria for an autism spectrum disorder who do not receive an explicit diagnosis – those individuals with moderate to severe intellectual disability or those with an already identified pre-existing associated medical condition, such as fragile X or tuberous sclerosis. One final caveat is that the studies summarised in Table 1 largely come from expert research clinical centres specifically studying young cohorts of children. In community settings in many countries there is evidence that for many children and their families a diagnosis is not confirmed until children are well into the school age years [55,56].

Variability and understanding individual trajectories in development

One feature that emerges from the longitudinal studies described above is that, aside from the issue of diagnostic or categorical stability, the developmental trajectory of symptoms measured using a continuous or dimensional (as opposed to a

categorical) metric changes over time. For example, Charman and colleagues [42] described how the trajectories of the social, communication and repetitive domain scores on the ADI-R had different developmental trajectories over time, consistent with the notion that the various aspects that make up the autism phenotype might not be tied together as closely as suggested by the current classification systems. This notion has also received support from a twin study demonstrating that, whilst each component of the autism phenotype is highly heritable, there is only very modest commonality in the heritability of the three components [57]. The recognition that autism is a complex neurodevelopmental condition and that the presentation changes (in different ways; in different individuals) over time presents considerable challenges to genetic and neuroscientific investigations. Longitudinal studies tracing the behavioural autism phenotype will therefore be important not just for informing clinicians regarding diagnostic practice but also for answering basic science questions regarding influences on the aetiology and course of the disorder.

Many studies over the past 20 years have demonstrated the perhaps unsurprising fact that over time individual variability is relatively stable in cohorts of preschoolers with autism – that is, for example, early language competence predicts later language competence – including in some studies that followed children into the school age period (e.g. [42,58,59,54,60]). However, theoretically more interesting has been the question of whether earlier-emerging social communication abilities predict later language development. A strong psycholinguistic tradition from the study of normative language development has shown that this is the case for typically developing infants and toddlers [61,62,63,64]. Given that many preschoolers with autism spectrum disorders are impaired in their development of language ability and of early social communication abilities, the question of whether such associations also

hold for toddlers and preschoolers with autism is both of clinical but also of theoretical interest. Demonstrating that the same association holds between early social communication abilities and later language development might suggest that similar developmental mechanisms are operating – albeit at a slower rate than in the typical case.

Mundy and colleagues [59] were the first to provide evidence to support this position finding that joint attention behaviours (alternating gaze, pointing, showing and gaze following) measured at 45 months were associated with language outcomes 13 months later. Sigman and Ruskin [54] extended this finding by demonstrating associations from the preschool years to later language ability at 12 years of age. Stone and colleagues have also demonstrated longitudinal associations between various aspects of imitation and play as well as joint attention abilities at 2 years of age and language abilities measured at 4 years of age. This pattern has now been replicated in several other studies (e.g. [65]), including one that followed children with autism spectrum disorders from toddlerhood (20 months) into the preschool years (42 months; [66]).

These findings are both of theoretical and practical importance. Theoretically, they suggest that since some of the associations seen in preschoolers with autism spectrum disorders are similar to that seen in typical development it might be the case that the mechanisms that operate are similar too. This is relevant to informing approaches to communication-based approaches to intervention (see below). Although individual stability of skills (language to language) or of one ‘precursor’ skill to another later emerging skill (joint attention to language [67]) may tell us something about intrinsic characteristics of the child, they may also suggest routes to intervention. Evidence consistent with this proposition was provided by Siller and

Sigman [68,69] who demonstrated that individual differences in maternal synchronicity (sometimes called ‘sensitivity’) measured in joint play interactions was associated with later language outcomes even over many years.

Developmental intervention approaches to enhancing social communication

The need for evidence that short-term, community-delivered early intervention programmes are effective is a priority. It is now recognised that up to 1% of children have an autism spectrum disorder [70,71]. Although presentation and outcome for individuals on the autism spectrum is very variable, in many cases it is a lifelong condition that is associated with significant morbidity and costs for the individual, their family and society as a whole. Recent estimates put the annual cost of autism spectrum disorder in the UK at £28 billion (~\$42 billion) [72]. In many countries the growing number of young, diagnosed children exceeds the capacity of available services [73,74,75]. This increase in service utilization challenges both researchers and service providers to develop systematic and effective dissemination strategies for transporting efficacious intervention procedures from university research to community service programmes.

The research evidence-base supports the use of behavioural, developmental and social-communication approaches for preschool children with autism (see [76,77,78,79,80]; for reviews). However, the number of well-controlled studies that employ randomised designs, that are the best protection against bias and spurious findings, are far and few between; although several promising approaches have been more rigorously tested in the past few years. In recent years a number of well-controlled intervention trials have focused on promoting and enhancing social communication and language skills. These have used a variety of social-communication and behavioural strategies, including the promotion of joint attention,

imitation and joint social engagement skills both directly delivered by therapists [81,82,83,84] and delivered by training parents in these methods[85,36], and found that language, developmental and social outcomes can be improved.

As described above, it is well-established that deficits in joint attention and symbolic play are among the earliest signs of developmental abnormality shown by young children with ASD. A recent randomised controlled trial by Kasari and colleagues [82,83] have demonstrated the effectiveness of short term interventions to enhance joint attention (JA) or symbolic play (SP) in children who were already receiving early, intensive behavioural intervention. Both the JA and SP groups showed significant improvements in expressive language but other changes were specific to the intervention received. Thus, children in the JA group made most improvement in joint attention and initiation; those in the SP group made more gains in symbolic and interactive play. At one year follow-up both intervention groups showed improved language and interaction skills, compared to controls [83], in line with longitudinal studies that show developmental relations over time between joint attention and play and language in preschool children with ASD [86].

Other interventions with a specific focus on early parent-child interaction and communication include the Hanen “More than Words” programme [87]. This has been shown to result in increased vocabulary and communication skills and a reduction in behavioural problems in the children involved and parents report improved coping skills and a reduction in stress [88]. Several other programmes are based on similar principles to “More than Words” – that is having a focus on shared attention and parental sensitivity to the child’s communicative attempts, with the goal of enhancing communicative exchanges to promote communication understanding and social engagement. A small scale randomized trial of the “Child’s Talk” programme [89] found that, compared to treatment-as-usual controls, parents in the

experimental group showed improvements in synchrony; their children showed decreases in autism severity and increases in initiations, reciprocal social interaction and vocabulary [85]. The Responsivity Prelinguistic Milieu Teaching (RPMT) model [84,90] also focuses on helping parents to learn to follow the child's lead, on increasing motivation to communicate, and using social games to provide natural reinforcement. RPMT has been shown to have positive effects on joint attention, turn taking and child initiations.

Another promising manualised intervention programme is the Early Start Denver Model (ESDM [91]) that combines aspects of developmental, behavioural, pivotal response and social-communication approaches. The ESDM's curriculum and teaching practices are manualised and draw extensively from previous work in two well-known, empirically supported models: (a) the Denver Model, a relationship and play based, developmental intervention relying on affective exchanges, shown to accelerate learning across a variety of developmental domains [92,93]; and (b) Pivotal Response Training [94], the naturalistic application of applied behaviour analysis aimed at optimizing child motivation to increase communication, language and play skills under natural conditions that more closely resemble the way typically developing children acquire developmentally appropriate skills [95,96].

In a landmark study that randomised forty eight 24 month olds with ASD into an ESDM group and 'treatment as usual' group, Dawson, Rogers and colleagues [81] reported that following 2 years of 15 hours per week therapy (with parents interacting with their child each week for approximately the same time as the therapists) developmental outcomes were significantly greater in the ESDM group compared to controls. The most striking differences were on the language subscales of the MSEL, which sits well with the authors' description of the ESDM as "an intervention

approach that uses teaching strategies of ABA that are delivered within an affectively rich, relationship-focused context” (Dawson et al., [81]; p.e23).

Final comments

For developmentalists, this convergence of evidence that for preschool children with autism spectrum disorders there are both naturalistic associations over time between early social communication skills and later language outcomes, and that these can be altered by targeted intervention in controlled studies, is as close to evidence for a *development mechanism* as it is possible to get [97]. There are still, however, many critical outstanding issues that need to be answered. In every treatment trial variability in outcome is considered and whilst some children make great gains, other make less progress and (at least in the trials which I have been involved in) some children make very little progress at all. Trials are the best (in many ways the only) context in which one can conduct rigorous analysis of moderating (which children do well?) and mediating factors (why do children make progress?). Answers to such questions from ongoing and future studies will allow us to fit treatments better to individual treatments, as well as to identify the effective elements of a particular approach.

The last decade has seen the publication of many important longitudinal and intervention studies and these have contributed to our understanding of autism as a developmental disorder. The challenge that lies ahead in the coming decade is for us to turn this understanding into developmentally informed treatment approaches and test them in rigorous and unbiased intervention trials.

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Table 1 Studies of diagnostic stability from preschool into the school age years

Reference	Age Time 1	Age Time 2	Diagnoses at Time 1	Findings
Lord (1995)	31 months	50 months	16 CA, 14 NS	Diagnosis largely stable; Clinical judgement more reliable than ADI-R
Stone et al. (1999)	31 months	45 months	25 CA, 12 ASD, 8 NS	CA diagnosis largely stable; ASD less so (4 out of 12 moved to NS at Time 2); Fewer repetitive symptoms at Time 1
Cox et al. (1999)	21 months	45 months	9 CA, 3 ASD, 31 NS	CA diagnosis largely stable; NS less so (7 out of 31 moved to ASD at Time 2); Fewer repetitive symptoms at Time 1; Clinical judgement more reliable than ADI-R
Moore & Goodwin (2003)	34 months	53 months	16 CA, 3 ASD, 1 NS	Diagnosis stable (slight movement between CA and ASD only)
Charman et al. (2005)	25 months	85 months	26 CA	Diagnosis largely stable (3 moved to ASD and 1 to NS at Time 2)
Turner et al. (2006)	31 months	109 months	18 CA, 7 ASD	Diagnosis largely stable (2 CA moved to NS and 1 ASD moved to NS at Time 2)
Lord et al. (2006)	29 months	112 months	84 CA, 46 ASD, 42 NS	Diagnosis of CA largely stable (12 from 84 moved to ASD and 1 to NS at Time 2); ASD less so (27 of 46 moved to CA and 5 to NS at Time 2); NS less so (2 from 42 moved to CA and 9 to ASD at Time 2)
Chawarska et al. (2007).	22 months	36 months	19 CA, 9 ASD	Diagnosis of ASD stable (2 of 19 CA cases moved to ASD at Time 2); Clinical judgement more reliable than ADI-R and ADOS-G
Turner & Stone (2007)	29 months	53 months	38 CA, 10 ASD	Diagnosis stability moderate only (6 of 38 CA cases moved to ASD and 13 moved to NS at Time 2; 6 of 10 cases of ASD moved to NS at Time 2)
Kleinman et al.	27 months	53 months	46 CA, 15 ASD, 16 NS	Diagnosis stability moderate only (15 of 61 ASD cases

(2008)				moved to NS at Time 2)
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CA = ICD-10 childhood autism/DSM-IV autistic disorder; ASD = PDD-NOS, atypical autism; NS = non spectrum