RUNNING HEAD: Rethinking the clinical pathway for autism

Rethinking the clinical pathway for autism spectrum disorder: Challenging the status quo

Abstract

Autism Spectrum Disorder (ASD) is typically diagnosed between 2 and 5 years of age, which is currently thought to be the earliest that the behavioural symptoms are able to be identified without ambiguity. A significant problem with this relatively 'late' age of diagnosis is that by the time a child has been identified and diagnosed with ASD, many of the best opportunities for therapies to capitalise upon brain plasticity very early in development are not realised. This paper provides an overview of the benefits and drawbacks of the current clinical pathway that places primacy on a diagnostic assessment for triggering the commencement of therapy. The paper then presents an alternative clinical pathway – the identification and provision of therapy to infants at risk of ASD – and provides a critical review of current evidence supporting this model. The aim of the paper is to outline a vision for the future of early identification and intervention of individuals with ASD, and the research goals that need to be addressed to achieve this vision.

Introduction

Autism Spectrum Disorder (ASD) is the collective term for neurodevelopmental disabilities characterised by impairments in social interaction, verbal and nonverbal communication and by repetitive patterns of behaviour (American Psychiatric Association, 2013). Comorbidities are common among individuals with ASD, and can include clinically significant difficulties in a range of neurocognitive domains, such as attention, cognitive and adaptive skills, as well as medical conditions, such as epilepsy, sleep and gut disorders. Symptom severity varies but, at a minimum, ASD compromises quality of daily living (Howlin, Good, Hutton & Rutter, 2004; Whitehouse, Watt, Line, & Bishop, 2009) and inter-personal relationships (Whitehouse, Durkin, Jaquet & Ziatas, 2009), with longer-term effects on educational and vocational attainment (Whitehouse, Line, Watt & Bishop, 2009), mental health (Simonoff et al., 2008) and family cohesion (Higgins, Bailey & Pearce, 2005).

Although ASD is generally considered a life-long condition, there is accumulating evidence that early and intensive intervention can reduce the severity of the social, communication and adaptive disabilities associated with the condition (Helt et al., 2008). A growing body of empirical studies indicate that the second year of life is a particularly important period of neurodevelopment, during which interventions for ASD may have maximum effect (Zwaigenbaum et al., 2015a). This period is not only a period of substantial neural plasticity that can be exploited by interventions (Dawson, 2008), but is also the age at which neurodevelopmental differences in brain growth (Redcay & Courchesne, 2005) and connectivity (Lewis et al., 2014) have been observed in infants later diagnosed with ASD. Clinical intervention research has focus primarily on three broad areas: therapy programs using behavioural principles to improve learning (e.g. Applied Behavioural Analysis, Lovaas, 1987); those using developmental and educational strategies (e.g. Treatment and Education of Autistic and Communication Handicapped Children; Schopler, 1997); and those with a specific focus on communication (e.g. Picture Exchange Communication System, Bondy & Frost, 1998). Models that employ strategies across these broad areas have also been developed in recent years (e.g. Early Start Denver Model; Dawson et al., 2010). Therapeutic intervention commencing at an early age is amongst the strongest predictors of a positive treatment response for individuals with ASD (Harris & Handleman, 2000), albeit with considerable variability in treatment response between individuals (Helt et al., 2008).

Speech-Language Pathologists (SLPs) play a prominent role in the clinical identification, assessment and management of individuals with ASD. Delays in early language development are commonly the first cause for concern among caregivers of children later diagnosed with ASD (De Giacomo & Fombonne, 1998), which often places SLPs as the first health professional to identify autistic symptomatology in young children. SLPs also play a crucial role in diagnostic assessments for ASD, particularly in the appraisal of the social communication difficulties that are a prominent feature of the diagnostic criteria (Glasson et al., 2008). The communication impairments characteristic of ASD often persist across the life-course, and the development of verbal and nonverbal communication skills is

often identified in surveys of individuals with ASD and their families as a key priority for therapy (Pituch et al., 2011; Rodger, Braithwaite, & Keen, 2004).

A common clinical pathway for the identification, assessment and management of ASD during early childhood (Camarata, 2014) is presented in Figure 1a. In this clinical pathway, children are often identified as developing differently by parents or early childhood professionals in the first two years of life (Young, Brewer, & Pattison, 2003). Caregivers may receive a clinical referral for their infant to undergo further assessment, or they may be advised to 'wait and see' if these developmental problems endure as the child gets older (Crane, Chester, Goddard, Henry, & Hill, 2015; Goin-Kochel, Mackintosh, & Myers, 2006). Children are most commonly referred for diagnostic assessments for ASD between the ages of 2 and 5 years (Daniels & Mandell, 2013), with the median age of diagnosis for ASD in Australia being 4.5 years (Bent, Dissanayake, Barbaro, 2015). In this clinical pathway, it is only after a clinical diagnosis of ASD is given to a child that intervention typically commences in earnest (Roberts & Williams, 2015)

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There are currently several drivers reinforcing the clinical pathway outlined in Figure 1a. First, the clinical presentation of individuals with ASD is highly variable and it has proven extremely challenging to identify clear and consistent diagnostic markers of ASD in children who are less than 12 months of age (Jones, Gliga, Bedord, Charman, & Johnson, 2014). The age of referral and diagnosis in ASD reflects the earliest age that the behavioural symptoms of the condition are currently thought to be able to be identified without ambiguity (Zwaigenbaum et al., 2015). Second, in many jurisdictions around the world, a clinical diagnosis is used to determine eligibility for support services. Therapeutic services for children with ASD are often highly time-intensive and come at considerable financial expense (Horlin, Falkmer, Parsons, Albrecht, Falkmer, 2014). Numerous governments around the world have responded to this need by developing schemes providing financial support to affected families, such as the Helping Children with Autism program provided by the Commonwealth Government of Australia. Eligibility for these schemes typically relies on a child possessing a clinical diagnosis of ASD, which has the effect of reinforcing the primacy of a diagnosis in the clinical pathway.

This clinical pathway presents clinicians with a paradox: on the one hand, there is evidence from both clinical (Helt et al., 2008) and basic science (Lewis et al., 2014; Redcay & Courchesne, 2005) demonstrating the importance of intervention during the first two years of life for promoting positive long-term outcomes; while on the other hand, there remains a strong clinical reliance on diagnostic assessments (which often occur after 2 years of age) to trigger the commencement of this intervention. The aim of the current paper is to challenge the primacy of an ASD diagnosis in the clinical pathway presented in Figure 1a by exploring the history and research underpinning the ASD concept. An alternative clinical pathway for ASD will then be presented - the provision of therapy to

infants showing behavioural risk factors for ASD (Figure 1b) – along with the research and practical challenges that must be overcome to implement this pathway into clinical practice. The paper will then provide a critical appraisal of research that has examined the identification and intervention of infants at risk of ASD during the second year of life.

An ASD diagnosis

The primacy of a diagnostic assessment in the existing clinical pathway for ASD infers that there is a clinical benefit in delaying intervention until there is certainty around the diagnostic status of the child. This view maintains that a diagnosis of ASD provides understanding of the biological and cognitive differences that lead to autistic behaviours, and that this knowledge helps clinicians better target therapies to promote positive long-term outcomes. However, this view can be challenged with an understanding of the evolution of the ASD concept over time, as well as through research insights that have revealed the behavioural and aetiological variability that exists under the ASD diagnostic label.

Medical conditions are typically diagnosed based on clear biological observations, such as the measurement of fasting blood sugar levels for a diagnosis of diabetes, or a suite of urine tests for kidney disease. By contrast, diagnoses of neurodevelopmental disorders such as ASD are based on behavioural observations only. ASD was first recognised in the early 1940s (Kanner, 1943), but was only introduced as a diagnostic category in the third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III, published in 1980) as Infantile Autism, which described a highly constrained behavioural phenotype characterised by relatively severe symptomatology and an age threshold for when these behaviours must have first emerged (American Psychiatric Association, 1980). Subsequent research identified that individuals who are less severely affected in terms of language ability and IQ may also present with the behavioural characteristics of ASD (Bishop, 1989; Georgiades et al., 2007), and more recent versions of the DSM incorporated flexibility into the behavioural requirements for a diagnosis. DSM-IV (American Psychiatric Association, 1994) introduced the category of Autistic Disorder, which listed 12 criteria across three behavioural domains: social impairments, communication difficulties, and restricted and repetitive behaviours and interests (RRBI). Individuals were deemed to meet the diagnostic threshold if they demonstrated at least 6 criteria, with a minimum of two criteria in the social domain, and one each in the communication and RRBI domain. DSM-IV also introduced two related diagnostic categories - Asperger's Disorder and Pervasive Developmental Disorder – Not Otherwise specified (PDD-NOS) – designed to account for the full spectrum of behaviours experienced by individuals displaying autistic behaviours. The DSM-5 (American Psychiatric Association, 2013) included several significant changes to the DSM-IV diagnostic categories. First, the diagnoses of Autistic Disorder, Asperger's Disorder and PDD-NOS were combined into the omnibus diagnosis category of Autism Spectrum Disorder. Second, the behavioural domains of social impairment and communication difficulties were amalgamated to create the domain of social communication difficulties, which are appraised in conjunction with behaviours in the RRBI domain to form a diagnostic profile.

The changes over time to the diagnostic categories for ASD emphasise not only an evolution in the understanding of the ASD concept, but also the large range of behaviours that exist under this conceptual umbrella. Like most human phenotypes, the social communication and RRBI behaviours that comprise an ASD diagnosis are dimensional and continuously distributed within the general population (Ronald et al., 2006). Population-based studies that have identified a smooth continuum of autistic behaviours have found no evidence of a sharp dividing line between clinical ASD and the broader population (Whitehouse, Hickey & Ronald, 2011). Numerous studies have also identified considerable behavioural overlap between ASD and other neurodevelopmental disorders, such as developmental language disorders (Whitehouse, Barry & Bishop, 2007, 2008), intellectual disability (Matson & Shoemaker, 2009), and attention deficit hyperactivity disorder (Ronald, Simonoff, Kuntsi, Asherson, & Plomin, 2008). The high prevalence of these conditions in the ASD population has led to widespread acceptance that 'pure' ASD – that is, individuals presenting with no behavioural features of other neurodevelopmental disorders – are the exception rather than the rule (Simonoff et al., 2008). The substantial clinical variability observed in ASD encourage a conceptual understanding of an ASD diagnosis as representing individuals with behaviours that are quantitatively different but not categorically distinct from the broader population (Bishop & Rutter, 2008).

Considerable variability between individuals has also emerged from the large body of research that has examined potential aetiological pathways underpinning ASD. The first major breakthrough in the understanding of the causes of ASD came through twin studies, which revealed a substantial genetic component to the condition. Folstein and Rutter (1977) examined 11 identical and 10 fraternal twins across Great Britain, where at least one twin had autism. Identical (monozygotic) twins share all of their DNA with their co-twin, and, when they grew up in the same household, they are assumed to share all of their environment. Fraternal (dizygotic) twins also share all of the environment with their co-twin, but only around half of their DNA, just like non-twin siblings. The key statistic is 'concordance', which is the percentage chance that if one twin has a given trait (in this case, autism), the other twin will also have autism. If the concordance is higher for identical twins than fraternal twins, then we can say that the difference is due to the increased amount of genetic material shared by the identical twins. Folstein and Rutter found the concordance for autism among identical twins was 36%, which compared to 0% for the fraternal twins. While the study was small in size, it provided the first evidence that ASD may be genetic in origin. Since the publication of this study, there have been over a dozen further twin studies (Ronald & Hoekstra, 2014), which have confirmed this original observation. The best current estimate is that there is a 50-80% concordance for identical twins, and a 5-20% concordance for fraternal twins, which indicates a strong genetic component to the condition (Ronald & Hoekstra, 2014).

The discovery of the heritability of ASD created scientific optimism that a single genetic factor may lead to the behaviours that characterise autism (Kim & State, 2014). However, several decades of intense genetic investigation had led researchers to the conclusion that there is no single genetic cause that is common to all individuals with ASD (Jeste & Geschwind, 2014). Genetic variants differ in

terms of their nature and frequency of occurrence in the general population. Inherited genetic variants, which are passed from a parent to an offspring, can occur at all frequencies, from rare to frequent. *De novo* variants, which are not inherited from parents and are newly occurring in the offspring, are mostly very rare. A number of large scale studies have found that the genetic variants that contribute to ASD can span all frequencies and can be both inherited and *de novo* (Robinson, Neale, & Hyman, 2015). A similar degree of heterogeneity in the neuroanatomy of individuals with ASD has also been observed (Amaral, Schumann & Nordahl, 2008). For example, several studies have reported evidence that individuals with an ASD diagnosis have atypical growth of the amygdala during early life (Sparks et al. 2002) and a reduction in the size of the corpus callosum (Lefebvre, Beggiato, & Bourgeron, 2015). However, not every individual with ASD has differences in the size or pattern of growth of the amygdala or corpus callosum, and for those individuals who do, it is unclear how this may relate to their autistic behaviours (Anagnostou & Taylor, 2011).

In summary, after more than seven decades of intense research, it is clear that neither the behavioural nor aetiological characteristics of ASD conform to a categorical diagnostic boundary. For this reason, the scholarly literature has seen a move away from conceptualising ASD as a unitary disorder with a large spectrum of behaviours, to viewing the condition as a syndrome of multiple and separate disorders, all with a relatively similar cluster of behavioural symptoms; that is, recasting autism and the autisms (Whitehouse & Stanley, 2013). This evolution in our understanding of ASD – a move towards interpreting the ASD label as a descriptive term for a broad range of behaviours, and away from the view of a behaviourally and biologically homogenous clinical population - is critical to placing into context the role of a diagnostic assessment in the clinical pathway for ASD. There is a large literature outlining the benefits of the receipt of a clinical diagnosis to individuals with ASD and their families, in terms of a greater understanding of behaviours and clarity about potential future needs (Mansell & Morris, 2004). However, the behavioural and aetiological variability encapsulated under the diagnostic label, means that a diagnosis of ASD in and of itself may not necessarily provide the strong platform on which to base clinical decision-making that is inferred from the clinical pathway outlined in Figure 1a. In essence, the clinical benefits to a child with ASD of waiting for diagnostic certainty to inform future intervention may be outweighed by the benefits of commencing interventions at an earlier, but diagnostically uncertain, age.

An alternative clinical pathway for ASD

An alternative clinical pathway for children with ASD is presented in Figure 1b. In this pathway, the trigger for commencing early intervention moves forward from the point of diagnosis (typically between 2 and 5 years of age) to the identification of 'risk markers' for ASD during the first two years of life. While a diagnostic assessment remains an important element of the clinical pathway, priority is placed on identifying children at increased risk of ASD as young as possible and providing intervention during a period of maximal neural plasticity (Dawson, 2008).

The key difference encompassed within this alternative clinical pathway is the commencement of early and intensive intervention during infancy, prior to the receipt of a clinical diagnosis for ASD. Early child development is known to be highly variable, and there are currently no clinical markers during infancy that are wholly predictive of a later diagnosis of ASD. It is therefore inevitable in this clinical model that intervention will be provided to a proportion of infants who would never have been on a developmental trajectory for ASD. A model that prioritises early intervention over diagnostic certainty presents two pragmatic challenges. The first challenge is ethical. All clinical interventions have accompanying costs, either in the form of side-effects (most often in the case of medications) or in the form of time and/or financial expenses. A treatment can only be ethically recommended when the improvement in symptoms outweighs the cumulative costs. Any pathway that involves the application of a clinical intervention to individuals who may not have a clinical need, must ensure that the cumulative costs to intervention recipients is low. The second challenge is economic. Behavioural intervention for neurodevelopmental disorders is expensive (Horlin et al., 2014; Peters-Scheffer, Didden, Korzilius, & Matson, 2012), and providing these interventions to a broader pool of children, some of whom, in hindsight, may not have had a clinical need, provides additional financial burden to health systems with budgetary constraints. The adoption of the alternative clinical pathway is dependent on the development of interventions for which it can be demonstrated that the costs of providing intervention to a larger group of individuals are outweighed by the longer-term benefits to the smaller proportion of individuals who had genuine clinical need.

Central to overcoming these ethical and economic challenges is the scientific challenge of providing clarity around the best methods for clinical management of infants at risk of ASD. World-wide research has focused on two aims in particular: (1) the discovery of risk markers during the first two years of life that are predictive of a later diagnosis of ASD, and (2) the development of interventions that are acceptable to families, feasible for clinicians to implement, and efficacious in improving the development of infants at risk of ASD.

Very early identification of ASD

Both retrospective and prospective methodologies have been used to investigate infant behaviours that may be predictive of later ASD. Retrospective study designs typically ask parents of children with a diagnosis of ASD to recall the behaviours of their child during the first years of life. A major drawback of this approach is the influence of natural biases in recalling events several years previous, and even more objective methods, such as viewing home videos recorded during infancy, have been criticised for being selective and non-standardised snapshots of the infancy period (Palomo, Belinchon & Ozonoff, 2006).

To address these methodological weaknesses, the research field has turned to prospective studies of infants at high-familial risk of ASD. Approximately 20% of siblings of ASD probands receive a diagnosis themselves (Ozonoff et al., 2011), and a further 10-20% experience sub-clinical autistic symptoms: the so called 'broader autism phenotype' (Sucksmith et al., 2011). This compares to the

population prevalence for ASD of 1% (Elsabbagh, Divan et al., 2012). Prospectively studying the early development of infant siblings of individuals with ASD ('high risk' infants) substantially increases the chances that a given sample will include infants who are later diagnosed with ASD. To compare the behaviours of these infants to a typical developmental trajectory, a 'low risk' group of infants with no family history of ASD is often studied in parallel.

Studies of high-risk sibling cohorts are yet to identify reliable behavioural markers for ASD in infants less than 12 months of age. Preliminary evidence has been observed for a range of behaviours at 6-12 months of age that may predict a later diagnosis of ASD, including reduced social gaze (Bryson et al., 2007; Werner et al., 2000), lack of orienting to name being called (Bryson et al., 2007; Werner et al., 2000), sensory disturbances (Bryson et al., 2007), and qualitative differences in gesture use (Colgan et al., 2006). However, these findings have not always been replicated (Landa & Garrett-Mayer, 2006; Landa, Gross, & Stuart, & Bauman, 2012; Ozonoff et al., 2010), and there is considerable between-individual variation in longitudinal outcomes for infants presenting with these behaviours. Clinical guidelines indicate that there is currently an insufficient evidence base to use any of these behaviours as an early marker for ASD prior to 12 months of age (Zwaigenbaum et al., 2015a).

Studies of infants during the second year of life have revealed more consistent findings, and there are several behavioural markers that are considered established risk factors for a later diagnosis of ASD (Zwaigenbaum et al. 2015a). Reduced levels of social attention and communication have emerged as the most robust marker of early behavioural difference. Numerous studies have reported that a reduced or lack of response to name between 12 and 24 months of age can distinguish children later diagnosed with ASD from both typically developing children (Zwaigenbaum, 2005) and children with other forms of developmental delay (Wetherby et al., 2004). Differences in the early behaviours relating to joint attention - the use of verbal and/or nonverbal communication to orient the attention of another person to a shared event – have also been linked to a later diagnosis of ASD. Qualitative and quantitative differences in infants as young as 14 months in both the responding to (Yoder, Sone, Walden, & Malesa, 2009; Sullivan et al., 2007) and initiating of (Goldberg et al., 2005; Stone, McMahon, Yoder & Walden, 2007) joint attention have been found to be predictive of a later ASD diagnosis. Lab-based studies using eye-tracking technology have also identified that infants as young as 14 months of age have reduced orienting to meaningful social information, such as a preference to visually examine geometric shapes over photos of children's faces (Ozonoff et al., 2008; Pierce, Conant, Hazin, Stoner, & Desmond, 2011).

A number of non-communicative behaviours have also been identified as early risk markers for ASD. For example, Watt et al. (2008) found that atypical use of objects between 18 and 24 months of age, such as the lining up or unusual visual exploration of toys, is predictive of an ASD diagnosis, and not present in individuals later diagnosed with developmental delay. There is also evidence that the repetitive motor behaviours that characterise clinical ASD, such as finger flicking and hand flapping,

often emerge during the second year of life (Watt et al., 2008). More generalised delays with early gross and fine motor development have also been noted as having some predictive capabilities for ASD (Bhat, Galloway, & Landa, 2012; Bolton, Golding, Emond & Steer, 2012), though the specificity of these early problems to ASD is not fully understood (Zwaigenbaum et al., 2015a). Toddler temperament has also been the focus of considerable research, with evidence that high levels of emotional dysregulation and reduced attentional flexibility may characterise infants who go on to develop ASD (Clifford et al., 2008).

While this collective body of research provides evidence for a constellation of behaviours emerging during the second year that are predictive of a later diagnosis of ASD – lack of response to name, poor joint attentional behaviours, atypical toy play, poor motor development, and emotional dysregulation - a finding common to all studies in the area is the high degree of variation in the natural history of pre-diagnostic ASD behaviours. Unsurprisingly, the developmental pathways to ASD appear to be as diverse as the range of clinical presentations of individuals with diagnosed ASD. Given this heterogeneity, it appears unlikely that a single behavioural marker common to all children with ASD will ever be identified during the first two years of life (Zwaigenbaum et al., 2015a). One promising approach to address this problem is the use of cumulative risk indices that take into account an infant's full behavioural and biological profile. The outstanding research question is what combination of symptomatology, and at what age, may confer the greatest risk for a later diagnosis of ASD, and what are the best intervention approaches to assist the development of these infants.

Very early intervention for ASD

Empirical studies that have investigated different models of early intervention for ASD have primarily focused on children with an existing diagnosis, aged 3 years or older (Helt et al., 2008). However, over the past decade, there have been an accumulating number of studies that have investigated the efficacy of 'very early interventions' for children 2 years of age or younger, often prior to a diagnosis of ASD. A key methodological challenge in conducting these studies is how participants are selected to take part in a trial. As reviewed above, no one developmental pathway has been identified that is common to all children with ASD, and so selecting children to provide an adequate test of the experimental intervention is challenging, particularly within the finite time and financial resources of a research project. To address this problem, many studies have utilised a 'high-risk' familial design, enrolling infant siblings of children with ASD, irrespective of whether they present with behavioural symptoms. A drawback of this approach is that, while siblings are at increased risk of being diagnosed with ASD, the absolute risk remains relatively low (approximately 20%; Ozonoff et al., 2011). The dilution of the study sample for infants with genuine clinical need, leads to a significant reduction in statistical power and, if not adequately controlled, can compromise the ability to provide an adequate test of the intervention. A second challenge is ensuring that these interventions are developmentally appropriate for infants. Zwaigenbaum et al. (2015b) argue that it cannot be assumed that interventions developed for older children are also acceptable, feasible and/or efficacious for younger children, particularly given the vastly different contexts for learning across the lifespan.

Infants depend far more than older children on experiential learning within their own natural environment, such as through social play with caregivers, and there is a clear need to either modify existing intervention programs or develop new models to adapt to these contexts.

The intervention programs developed to date have focused on parent coaching as a method for improving the early social environment of infants. While genetic variation is known to play a major role in the aetiology of ASD (Jeste & Geschwind, 2014), there is emerging evidence that any risk susceptibility in brain and behavioural functioning caused by genetic factors may be exacerbated by poor-quality interactions within the social environment. The interactive specialisation theory of developmental neuroscience proposes that the quality of an infant's early social interactions has a major influence on the developing brain structures that underpin social behaviour (Johnson, 2011). Parent-infant interactions are critical in creating the optimal social environment that facilitates the development of neural pathways within the social brain system (Dawson, 2008). Parental interaction styles that are less directive and more sensitive to child cues are known to assist in the development of early social skills, and are associated with more favourable long-term communicative and social outcomes for children with typical (Tamis-LeMonda, Bornstein, & Baumwell, 2001) or atypical (Siller & Sigman, 2002) development.

Infants are typically born with biases to orient towards, attend to, and learn from social stimuli (Grossman & Johnson, 2007). By contrast, there is good evidence that infants later diagnosed with ASD have reduced or impaired function in one or more of the underlying biasing mechanisms early in life (Elsabbagh, Mercure et al., 2012; Whitehouse & Bishop, 2008). Disruption in social orienting among infants later diagnosed with ASD can lead to differences in parent-infant interaction styles. Parents of high-risk infants often exhibit less sensitivity to their infant's behavioural cues and increased directiveness, such as through behavioural prompting (Wan et al., 2013). While these poor interactional cycles are not the primary cause of the child's ASD, they may maintain or amplify a pre-existing biological vulnerability to ASD in the infant. This point in development provides an intervention opportunity for Speech-Language Pathologists, with the hypothesis that increasing the quality of parent-child interactions will improve the social environment of an infant early in development and alter the trajectory of disability in children with ASD.

Three small studies have provided evidence that optimising parent-infant interactions within the first year of life can enhance developmental outcomes for infants at high risk of ASD (Koegel, Singh, Koegel, Hollingsworth, & Bradshaw, 2013; Rogers et al., 2014; Steiner, Gengoux, Klin & Chawarska, 2013). However, each of these small-scale studies is at 'proof of concept' stage only, has included sample sizes of fewer than 10 infants, and was not a randomised test. Currently the most advanced line of research for infants at high-risk of ASD is iBASIS-VIPP, which uses video-feedback to help parents adapt to their infants' communication styles and promote optimal social and communicative development. In a series of home-based sessions, the SLP films parent-infant interactions and uses footage excerpts to improve parental understanding of the infant's communicative signals. An initial

case-series of eight infant siblings of children with ASD (aged 8-10 months) established the acceptability and feasibility of the intervention to parents and infants (Green et al., 2013). A follow-up investigation examined the intervention in the context of a two-arm, assessor-blinded randomised controlled trial (Green et al., 2015). Infant siblings of children with ASD were randomised to receive either 10 therapy sessions of iBASIS-VIPP over 5-months (n = 28) or no intervention (n = 26). Analysis of outcome assessments immediately post-treatment (mean age of 14 months) identified significant improvements in parental interaction styles promoting social communication development in their infants, as well as a non-significant trend towards reduced ASD risk behaviours as measured by the Autism Observation Scale for Infants. Data collected during follow-up assessments of these children at a later age have not yet been published.

Conclusion

ASD is diagnosed in at least 1% of individuals, making the condition among the most prevalent of all neurodevelopmental disorders. The model of clinical practice for ASD that has gained prominence over the past half a century has placed critical importance on a diagnostic assessment as the platform for informing treatment pathways. This model has been reinforced by eligibility for Government services typically requiring a diagnostic label, as well as the historical view that the diagnostic status of an individual provides a significant advantage in choosing therapy pathways. However, the now substantial research literature highlighting the behavioural and aetiological diversity encompassed within the ASD diagnostic label, draws into question the clinical value in waiting for a child to reach a diagnostic age of 2 years and above.

The current paper presented an alternative clinical pathway, which deemphasises the immediate importance of diagnostic certainty for children with developmental difficulties, and instead prioritises identification of infants at high risk of ASD during the second year of life and the immediate provision of intervention. A large body of research has investigated the developmental trajectories that may precede a diagnosis of ASD. A range of infant behaviours during the second year of life have been found to indicate risk for a later diagnosis of ASD – lack of response to name, poor joint attentional behaviours, atypical toy play, poor motor development, emotional dysregulation – but no one single behavioural marker is wholly predictive of ASD. Several studies have investigated the feasibility, acceptability and efficacy of parent-mediated interventions for infants at high-risk for ASD, with promising results observed for several therapy programs. However, there remain important challenges that need to be overcome before the adoption of this alternative pathway.

A pressing research goal is to identify which combination of behaviours during the second year of life may be the most predictive of diagnostic outcome and is both feasible and effective to use in the clinical context. Understanding which behavioural differences may optimise the key statistic of positive predictive validity – the probability that an infant displaying a certain set of behaviours will be diagnosed with ASD at a later age – is central to this goal. A second research goal is to quantify the behavioural, quality of life and economic gains that may result from the provision of very early

intervention commencing during the first two years of life. Understanding the full range of costs associated with the alternative clinical model in relation to the full range of benefits of earlier intervention (cost-benefit analysis), and then comparing this analysis with the existing clinical model (cost effectiveness), are essential in guiding decision-making within both private and public health systems.

Objective and regular evaluation of existing clinical practices is the duty of every clinician and clinical researcher. Acquiring the habit of questioning the evidence behind every aspect of the clinical pathway will inevitably lead to greater clinical skills and better outcomes for clients. At the heart of clinical research is the desire to challenge the status quo and determine if there is an evidence base to improve on existing methods. There is a growing research literature indicating that our existing clinical pathway for ASD may be improved through identification and intervention of 'high risk' infants during the second year of life. While the evidence base is not yet strong enough to warrant a shift to this new clinical model, the rapid pace of research growth in this area indicates that the Speech-Language Pathology profession may currently be standing on the precipice of a major clinical change.

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Figure captions

Figure 1

The current clinical pathway for autism spectrum disorder (ASD; Figure 1a, top panel) and an alternative clinical pathway (Figure 1b, bottom panel). The horizontal line denotes the age of the child and shading indicates the intensity of intervention provided.