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Early Detection of Autism Spectrum Disorders

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1. Introduction

Autism spectrum disorders (ASDs) are neurodevelopmental disorders characterized by distinctive language impairments, social and communicative deficits, and patterns of restricted and stereotyped behavior. In the Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision (DSM-IV-TR) (American Psychiatric Association, 2000), pervasive developmental disorders (PDDs) are also referred to as autistic disorder (AD), Asperger's disorder, PDD not otherwise specified (PDD-NOS), childhood disintegrative disorder, and Rett Disorder. However, the diagnostic boundaries between these PDD subtypes remain unclear, the symptoms and behaviours lie on a continuum and have considerable clinical heterogeneity (Szatmari, 1999). In this review, therefore, ASDs are referred to as the diagnostic category of PDDs.

2. Diagnosis of ASDs

The manifestations of ASDs vary from mild to severe and pervasive impairment. Currently, the diagnosis of ASDs is based on the criteria developed in the DSM-IV-TR and the International Classification of Diseases, 10th revision (ICD-10) (World Health Organization (WHO), 1992) and is supported by standardized diagnostic instruments. According to the DSM-IV-TR criteria, the impairments of ASDs consist of three main impairments which must all be presented for diagnosis.

2.1 Impairment in social interaction is defined by various symptoms including impairment in the use of nonverbal behaviours (e.g. eye contact, use of gestures and facial expressions); lack of showing, bringing or pointing out objects; odd relationships of approaches to others; and lack of social or emotional reciprocity.

2.2 Impairments in communication consist of delay in or total lack of spoken language, inability to initiate or sustain a conversation with others, stereotyped or repetitive use of language, and lack of social imitative play.

2.3 Restricted repetitive and stereotyped patterns are behaviours, interests and activities as manifested by an inability to cope with change, a dislike for any interruption to routine, preoccupation with specific subjects or activities, repetitive or stereotyped motor mannerisms such as hand flapping or twisting, and persistent preoccupation with parts of objects.

Early diagnosis for ASDs is undoubtedly important and is considered as a clinical best practice. Early detection of ASDs leads to an early intervention (Rutter et al., 2006).

However, diagnosis before the age of 3 years remains a challenge (Baron-Cohen et al., 1996). Some symptoms of ASDs may overlap with normal developmental variance. Also, ASDs are a continuum of disease which has a wide range of individual differences. Distinctions between autistic disorder and PDD-NOS remain unstable. A study reported that up to 50% of PDD-NOS cases, who were diagnosed before age 3 years, could have been overdiagnosed, whereas around 22% were underdiagnosed (Chawarska et al., 2007). This was due to the fact that diagnosis depends on clinical judgments which sometimes may not agree with the DSM-IV-TR diagnostic criteria especially evaluating a young child. Some of the criteria in the DSM-IV-TR can not apply to young children. In other words, many of the characteristic behaviours in the DSM-IV-TR are not apparent before 36 months. For example, a child age less than 16-month-old typically can engage in parallel play but has not yet developed reciprocal peer relationships. Thus, the criteria of failure to develop age-appropriate peer relationships need to be adapted (Martinez-Pedraza & Carter, 2009). The criteria of stereotyped and repetitive use of language can be difficult to discriminate between repetitions of the last word in young typically developing children and echolalia in children with ASDs. Furthermore, the criteria “restricted repetitive and stereotyped patterns of behaviour, interests and activities” may not appear in young children. These may appear later after the third birthday in some cases (Gray & Tonge, 2001; Turner, 1999). Therefore, making a diagnosis in children younger than 2 years of age is very challenging.

3. Early signs of ASDs

Many research studies have concluded that the first signs and symptoms of ASDs are evident by 12 to 18 months of age (De Giacomo & Fombonne, 1998; Young et al., 2003). Research on early signs and symptoms of ASDs in young children have focused on parental retrospective reports, early home videos of children later diagnosed with ASDs, and studies on siblings of children with ASDs. The emergence of ASDs signs and symptoms involve the area of social skill deficits, language skill deficits and unusual repetitive or stereotypical behavioural patterns. Signs and symptoms that are predictive of ASDs in young children are, namely:

3.1 Social skills deficits

Social skills are one of the most important areas in defining ASDs in very young children. In typically developing children, social development is acquired parallel to overall development (e.g. language, motor and cognitive development). In the very young children whose language skills are limited, social development depends very much on clinical observations. The manifestation is a lack of or a decreased drive to connect with others, including share feelings, thoughts and actions. Children who have ASDs have limited or reduced eye contact, fail to orient their name being called, limited imitation, limited responding to reciprocal social games, and lack of showing or bringing an object to a caregiver.

The important characteristic in helping make a diagnosis in very young children is lack of “joint attention” (JA) (Charman, 2003; Dawson et al., 2002; Turner et al., 2006). JA refers to the capacity of the child to coordinate attention with a social partner in relation to an object or event (Rapin & Tuchman, 2008). JA normally appears to develop between 8-16 months. In 8-10 months old typically developing children, the child will follow the caregiver’s gaze

when the caregiver looks at an object or event. This development milestone is called “gaze monitoring”. Around 10-12 months of age the child can follow the caregiver’s point and can look back at the caregiver. At approximately 12-14 months the child will request for objects by pointing. In detail, the child will look back and forth between the object and caregiver to reassure that the caregiver understands his or her need, so called protoimperative pointing. At 14-16 months when the protodeclarative pointing develops, the child will look alternatively between the object and the caregiver. The goal is to share social experience, not the desired object (Johnson & Myers, 2007). Other nonverbal gestures, including facial expression, usually help discriminate the difference between these two types of pointing. Children with ASDs can not achieve these skills at an age-expected time or some can achieve partially but do not qualitatively achieve the skill completely. Some children may have no pointing at all but use their caregivers’ hands point to the desired object. Some children look at the object but do not look at the caregiver to connect socially. A study in infant siblings of children with ASDs stated that the inability to shift one’s attention (between child, parent and object) may be the first reliable sign of ASDs (Zwaigenbaum et al., 2005). In brief, lack of or delayed JA skill that is discrepant from overall functioning is a core feature of the ASDs diagnosis.

Since JA skills may not be observed in typically developing children younger than 1 year of age, responding to their name being called is a skill that the child should achieve. Children with ASDs usually fail to respond to their name being called. Some children with ASDs may respond to environmental sounds well enough to reassure the caregivers that their children can hear. Home videos of 1-year-old children who later were diagnosed with ASDs found that orienting to name being called is one of the most consistent deficits for affected children at that age (Baranek, 1999; Osterling & Dawson, 1994).

Delay in play skills is one of the features associated with diagnosis of ASDs. In respective order, play starts with sensory-motor, functional, constructive, and pretend or imaginary play. In typically developing children, approximately 4 months old, sensory-motor play begins. At 12-14 months of age, the child plays in a more functional manner. Pretend play starts around 16-18 months of age and increases gradually in complexity. Lack of or delay in pretend play or play that never passes the sensory-motor play stage serves as a distinguishing characteristic of ASDs. Although, some children with ASDs progress to functional play, the quality of play is significantly different from typically developing children by around age 2 years i.e. play is less purposeful, less symbolic and less in complexity (McDonough et al., 1997; Sigman et al., 1999; Stone et al., 1990). Some children with ASDs play or manipulate objects in a stereotypic or ritualistic manner such as lining up, banging, and mouthing objects. They usually prefer playing alone and have trouble incorporating into social play. This sophisticated social play may not develop which further worsen social skills development.

Although, there is a possibility to detect social skills deficits in children younger than 1 year of age, the reliability remain problematic before 18 months (Rutter, 2006). Special consideration should focus on gaze monitoring, joint attention, responding to being called by name, and play skills.

3.2 Early language skills deficits

Generally, absence of language skills appears at around age 2, which may lead to diagnosis of ASDs. In order to diagnose of ASDs earlier, delay in language development should be

detected as soon as possible. A study among the siblings of children with ASDs demonstrated that during the first year of life, infants later diagnosed with autism vocalized less than low-risk control infants. Moreover, delays in verbal skills and early language comprehension were evident (Zwaigenbaum et al., 2005). Regarding language abnormalities, both expressive and receptive language deficits should be monitored. Typically, infants start to babble by 6 months of age, followed by advances in complexity which includes several phonemes. Later, jargoning (i.e. adds inflection to utterances in an attempt to tell a story) develops at approximately 10 -12 months of age. Lack or delay of an alternating to-and-fro pattern of vocalizations between infant and parent, delay of onset of babbling, and decrease or no use of pre-speech gestures (e.g. pointing, showing, nodding) are characteristic of ASDs (Wetherby et al., 2000; Johnson & Myers, 2007).

Repeating words in particular the last one or two words of a sentence right after being heard can be observed in typically developing children under the age of 2 years, which mimicks the ASDs symptom of immediate echolalia. However, the typically developing child will pass through this brief stage and will acquire functional language. In children with ASDs, this imitation still persists as expressive language after the age of around 2 years and beyond. Furthermore, the children with ASDs mostly repeat words in an odd intonation or repeat exactly the same intonation as they heard (Martinez-Pedraza & Carter, 2009).

In young children with ASDs, receptive language ability is often impaired. They initially do not respond to their names when called by a caregiver. After language is present, children with ASDs are unable to initiate or sustain conversation. Some children have comprehension deficits, particularly in complex sentences or questions. Children with ASDs also show deficits in non verbal communication; for example, they look at others less, have less social smile, lack appropriate gestures, have less pointing or have difficulty following a point, show objects less and have a lack of appropriate facial and emotional expression. These non verbal communication deficits are linked closely to lack of social skills development (Martinez-Pedraza & Carter, 2009).

There is approximately one fourth to one third of children with ASDs whose parents reported a significant loss or regression in language development. The regression characteristically occurs between 15-24 months of age (Lord et al., 2004; Luyster et al., 2005). Although, some parents reported normal development prior to regression, studies showed that some children with ASDs have subtle language and social impairments before the onset of regression (Richler et al., 2006; Werner & Dawson, 2005).

3.3 Restrictive interests, stereotypic and repetitive patterns of behaviours

Stereotypies and repetitive behaviours are not specific to children with ASDs. Children who have globally developmental delay (GDD) and children with sensory impairment may demonstrate stereotypies. Even in typically developing children, stereotypies may present e.g. flapping their hands when excited (Johnson, 2008). Stereotypies and repetitive behaviours in children with ASDs usually are not common in very young children (Charman & Baird, 2002; Cox et al., 1999; Moore & Goodson, 2003). Children with ASDs are preoccupied with sameness and routines, so interruption or changes in routine lead to tantrum and emotional disturbance. Some display sensory abnormalities: hypo- or hyper-responsive to sensory stimuli. Some children show an unusual and preoccupation with a topic of interest such as train schedules, solar system, dinosaurs, etc. However, this strong

interest may not present in young children with ASDs. These patterns of behaviours vary among young individuals with ASDs. Therefore, diagnosis of ASDs in very young children should focus on social skills and language skills deficits rather than stereotypies and repetitive behaviours.

4. Screening tools for ASDs

The American Academy of Pediatrics (AAP) recommends ASDs screening in children age 18 and 24 months as part of developmental surveillance during regular health visits (Johnson & Myers, 2007). There are many valuable screening tools designed, such as the Checklist for Autism in Toddlers (CHAT) (Baron-Cohen et al., 1992; Baron-Cohen et al., 1996), the Modified Checklist for Autism in Toddlers (M-CHAT) (Kleinman et al., 2008; Robins et al., 2001), the Screening Test for Autism in Two-Year-Olds (STAT) (Stone et al., 2000) and the Pervasive Developmental Disorders Screening Test-II (PDDST-II) (Siegel, 2004). All of these tools, except the STAT, are designed as first-level screens (i.e. the tools are administered to all children to differentiate children who are at risk of ASDs from the general population).

Baron-Cohen *et al* conducted a study using the CHAT to administer in a primary health care setting to identify 18-month-old children at risk of ASDs. The study included both direct observation and a questionnaire for parents. The CHAT focuses on 3 key items which are gaze monitoring, protodeclarative pointing and pretend play. Findings from the study in the general population demonstrated that, the CHAT had a specificity of 98%-100% and a sensitivity of 18%-38% (Baird et al., 2000; Baron-Cohen et al., 1992; Baron-Cohen et al., 1996; Scambler et al., 2001). Attempts to improve sensitivity by modifying the cut-off criteria resulted in decrease in positive predictive value (from 75% to 5%). Overall, use of the CHAT as a screening tool remains problematic owing to low sensitivity (Bryson et al., 2003).

The M-CHAT is a screening tool for children 16 to 48 months and was developed to improve prediction of the CHAT. In the M-CHAT, there is no observation component, but includes a wider range of signs and symptoms of ASDs. This parental questionnaire consists of 23 (yes-no) items. Children who fail any three items or two critical items are considered to be at risk for ASDs. Items that were found to be the best predictors for ASDs were protodeclarative pointing, response to name, interest in peers, bringing things to show parents, following a point, and imitation. The reported sensitivity and specificity of the M-CHAT were around 89% and 93%, respectively (Dumont-Mathieu & Fein, 2005). However, the positive predictive value (PPV) was low (0.11 ± 0.05) when it was used alone as a screen for ASDs in a community-based sample. The follow-up interview was reported to be able to significantly increase the PPV (Kleinman et al., 2008). Overall, the M-CHAT showed higher sensitivity than the CHAT and is possibly useful in identifying children in need of further assessments, but should not be used as a screen to exclude the possibility of ASDs (Eaves et al., 2006; Barbaro & Dissanayake, 2009).

The STAT is a second-level screen (that is, the tool is used to differentiate children who are at risk of ASDs from those at risk of other developmental disorders). It was designed to be used in children aged 2-3 years. The STAT includes 12 pass/fail items and is administered in a play-like setting in order to observe social-communicative behaviours. The test lasts approximately 20 minutes to complete. The estimated sensitivity and specificity were 95% and 73%, respectively (Stone et al., 2008). However, increased validity in larger studies and community-based samples are required.

The PDDST-II has both a first and second level screen versions. It is a parental questionnaire that can be used with children under 6 years of age. To date, the clinical validity remains unclear because it has not yet been published in a peer-reviewed journal (Volkmar et al., 2005).

5. Diagnostic instrument for ASDs

Currently, there are standardized instruments to facilitate diagnosis in ASDs. The Autism Diagnostic Interview – Revised (ADI-R) (Le Couteur et al., 2003; Lord et al., 1994) and the Autism Diagnostic Observation Schedule (ADOS) (Lord et al., 2000a) are well validated and currently their combination with clinical judgment based on the DSM-IV-TR criteria are considered as the “gold standard” for diagnosis of ASDs (Battaglia, 2007). However, these instruments should be used with caution in very young children or children with a mental age less than 24 months (Stone et al., 1999).

The ADOS is the most widely used standardized semistructured assessment of communication, social interaction and play. The scenarios for interaction with the child are used in the ADOS and require a well-trained interviewer. The ADOS consists of 4 modules devised for individuals with varying developmental and language level. Each module lasts approximately 40 minutes. The ADOS provides an algorithm to differentiate between autism, ASD and not ASD. Alpha coefficients are 0.86-0.91 for the social domain (across modules), 0.74-0.84 for communication, and 0.63-0.65 for repetitive behaviours (modules 1 and 2) (Lord et al., 2000a). In younger children, especially younger than 15 months of age, the sensitivity is excellent, the specificity is doubtful (Chawarska et al., 2007; Lord et al., 2000b; Risi et al., 2006). Luyster *et al* developed the toddler version of the ADOS (ADOS-Toddler Module or ADOS-T) which can be used for children under 30 months of age who have non-verbal mental ages of at least 12 months. The ADOS-T has acceptable internal consistency and excellent inter-rater and test-retest reliability (Luyster et al., 2009). However, larger samples of children and long follow-up studies need further replication.

The ADI-R is a standardized parental interview conducted by a trained interviewer. The interview covers the past developmental history and current functioning of individuals. The tool consists of 111 questions and takes about 2-3 hours. The ADI-R is designed to use in children about 4-5 years old. The ADI-R provides an algorithm to differentiate between autism and not autism. The ADI-R is reliable and valid. The inter-rater reliability on individual algorithm items ranges from 0.63 to 0.89. The internal consistency (alpha coefficients) is 0.69-0.95 (Lord et al., 1994). However, the time needed for administration precludes its use in clinical settings. Moreover, further study is needed for identifying ASDs in preschool children (Le Couteur et al., 2008; Mazefsky & Oswald, 2006; Risi et al., 2006).

The Developmental, Dimensional and Diagnostic Interview (3Di) is a new structured computerized interview for the diagnosis of ASDs and extends to co-morbid disorders. There are total 266 questions on autistic spectrum disorders (ASD) symptoms and 53 questions for an abbreviated interview. The questions in the interview are clustered according to domains of function: reciprocal social interaction skills, social expressiveness, use of language and other social communication skills, use of gesture and non-verbal play, and repetitive/stereotyped behaviours and routines. To reduce a risk of respondent bias, breaking down complex questions and scattering their components throughout the interview were done. A study reported that test-retest and inter-rater reliabilities were

excellent. The sensitivity and specificity were estimated about 100% and 97%, respectively. Both the original 3di and the short version demonstrated high agreement with the ADI-R (Santosh et al., 2009; Skuse et al., 2004). Moreover, the short version takes less time to perform compared with the ADI-R. However, the study was limited to mild cases of ASDs; and so far limited numbers of young children have been tested.

The Autism Observation Scale for Infants (AOSI) (Bryson et al., 2008) is a diagnostic instrument that was developed for infants aged 6-18 months. The instrument consists of 18-item direct observational measure. Various activities were developed to assess the infant's target behaviours. These target behaviours are visual tracking and attentional disengagement; coordination of eye gaze and action; imitation; early social-affective and communicative behaviours; behavioural reactivity; and various sensory-motor behaviours. The inter-rater reliability ranges from 0.68 to 0.94 at 6, 12 and 18 months. Test-retest reliability is acceptable. The AOSI takes approximately 20 minutes to administer. Although, the AOSI is a useful diagnostic instrument for young children, it is not yet proposed to be used.

In brief, although there have been a number of screening and diagnostic instruments to facilitate ASDs diagnosis, a comprehensive evaluation for suspected ASDs should be performed. Such evaluations include a developmental history, parental interview, thorough physical examinations, clinical observations, developmental evaluations, assessment of the strengths and weaknesses of the child, assessment of family functioning, administration of standardized diagnostic instruments that operationalize the DSM criteria, and measures of cognitive and adaptive functions. Such comprehensive approaches together with early detection can lead to early intervention and result in improvement of the long-term functioning of children with ASDs.

6. Summary

Early detection of ASDs provides the best opportunity for early intervention, which results in significantly improved outcomes for children with ASDs. Awareness of the importance of early diagnosis and treatment has increased attention on knowledge of the very early manifestations of ASDs. Early manifestations include abnormalities in social interaction, communication and behaviours. Firstly, regarding social interaction, a lack of eye contact, orienting to name call, imitation, joint attention and limited responding to reciprocal play skills are the markers that should be of concern. Secondly, in the area of communication, any lack or delay of communication skills including verbal and non-verbal communication are indicative signs of ASDs. Lastly, the abnormal or unusual behaviours (i.e. repetitive and stereotypic behaviours, restrictive interests, preoccupied with sameness/ routine and sensory abnormalities) can be apparent in young children, however, these behaviours may not serve as important predictors of ASDs as the social and communication impairments.

Although, there are screening instruments to help identify children with ASDs in community-based samples, there is no screening instrument that provides adequate sensitivity and specificity for universal screening (Barbaro & Dissanayake, 2009). According to standardized diagnostic instruments, there have been many studies showing that the ADI-R and the ADOS have been well validated and are the instruments to accurately diagnose ASDs as early as 2 years. The combination of the ADOS and the ADI-R in conjunction with clinical diagnosis based on the DSM-IV-TR are recommended when

diagnosing very young children with ASDs. In clinical practice where diagnostic instruments are not applicable, developmental surveillance with proper guidance is a recommended approach. Further prospective studies in young children should be conducted to provide evidence-based diagnosis for young children, especially under the age of two. Those developing research offer hope for better outcomes for children with ASDs.

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Estimated prevalence rates of autism spectrum disorders (ASDs) have increased at an alarming rate over the past decade; current estimates stand as high as 1 in 110 persons in the population with a higher ratio of affected males to females. In addition to their emotional impact on the affected persons and their family members (in fact, the latter are often unrecognized unaffected “patients” themselves), the economic and social impacts of ASDs on society are staggering. Persons with ASDs will need interdisciplinary approaches to complex treatment and life planning, including, but not limited to, special education, speech and language therapy, vocational skills training and rehabilitation, social skills training and cognitive remediation, in addition to pharmacotherapy. The current book highlights some of the recent research on nosology, etiology, and pathophysiology. Additionally, the book touches on the implications of new research for treatment and genetic counseling. Importantly, because the field is advancing rapidly, no book can be considered the final word or finished product; thus, the availability of open access rapid publication is a mechanism that will help to assure that readers remain current and up-to-date.

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