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Diagnosis and Assessment of Autism Spectrum Disorder in South Korea

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Autism spectrum disorder (ASD) is diagnosed by the clinical decision of a trained professional based on the Diagnostic and Statistical Manual for Mental Disorders, Fifth Edition or International Classification of Diseases 11th Revision diagnostic criteria. To obtain information for diagnostic formulation, professionals should explore detailed developmental history, and can use structured or semi-structured assessment tools to observe interaction between the child and parents or strangers. Diagnostic assessment should include a profile of the strength and weaknesses of the individual and should be conducted using an optimal approach by a multidisciplinary team with appropriate techniques and experience. Assessment of language, cognitive, neuropsychological, and adaptive functioning should be conducted in ASD individuals prior to establishing an individualized treatment plan. Genetic testing, brain magnetic resonance imaging or electroencephalogram testing can be considered for identification of underlying causes.

Keywords: Autism spectrum disorder; Diagnosis; Biomarker; Comorbidities; Differential diagnosis.

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GENERAL PRINCIPLES

The usual practice for children with developmental delays, behavioral problems, psychiatric problems, or genetic syndromes should include monitoring for autism spectrum disorder (ASD). ASD can be diagnosed by the clinical decision of a trained professional based on the Diagnostic and Statistical Manual for Mental Disorders, Fifth Edition or International Classification of Diseases 11th Revision diagnostic criteria [1]. To obtain information for diagnostic formulation, professionals should explore detailed developmental history, and use structured or semi-structured assessment tools to observe interaction between the child and parents or strangers [2]. As information on child behavior may differ across informants and is also situational, a complimentary assessment of developmental history from multiple informants and observation of child behavior across several appointments are necessary.

The purpose of a diagnosis is to provide adequate support and guidance to the patient and their family. The National Institute for Health and Care Excellence (NICE) guidelines state that "the focus of assessment should not only be on diagnosis, but also should consider the risks a person faces, as well as their physical, psychological and social functioning … in all cases the central aim is to identify the need for treatment and care" [3]. Therefore, integration of assessments by multidisciplinary professionals on the individual's symptoms, functioning level, and interaction with the environment is essential for diagnosis [4].

SCREENING TESTS

Screening tools are used to identify ASD high-risk individuals that require further diagnostic assessment [5]. Screening tools can be used for obtaining information, in combination with other sources of information for referral of ASD diagnostic tests. Screening tools should not be used as a solitary tool for ruling-out ASD. Screening tools available in Korea include the Modified Checklist for Autism in Toddlers (M-CHAT) [6], Social Communication Questionnaire (SCQ) [7], Social Responsiveness Scale (SRS) [8], and Behavior Development Screening for Toddlers (BeDevel) [9]. The purpose and age of testing, completion time should be considered when selecting screening tools (Supplementary Table 1 in the online-only Data Supplement) [6-8,10-13].

Despite the recommendation of regular developmental screening by the American Academy of Pediatrics [14], the

US Preventive Services Task Force cited that there is a lack of evidence supporting screening of ASD in the whole general population [15]. The PrevInfad workgroup (Spanish Association of Primary Care Pediatrics), the United Kingdom National Screening Committee and the Canadian Task Force on Preventive Healthcare recommends against universal screening, but for screening among children with high risk [16]. A targeted approach may be more appropriate compared to universal screening, like application of screening to younger siblings of ASD children, children recommended in-depth evaluation as a result of developmental surveillance, children with developmental delay, children who are suspected to have developmental delay by their education or day care center, and children whose parents express concern of development delay [17,18]. Opposite views were presented by Dai et al. [19], who reported the incremental utility of screening children for ASD at 18 and 24 months to maximize opportunities for early identification. In the Victorian province of Australia, all Maternal and Child Health (MCH) nurses are trained using the Social Attention and Communication Study (SACS) to monitor babies for ASD at their routine health checks between 12- and 24-months-of-age. A large-scale community-based study demonstrated high accuracy of SACS in infants, toddlers, and preschools, suggesting that the SACS should be used as part of a population-based, developmental surveillance program for the early identification of ASD within the general population [20].

In South Korea, developmental surveillance is administered 8 times from age 14 days to 71 months (age 6). The Korean Developmental Screening Test for Infants and Children (K-DST) is a developmental screening test that consists of 6 domains including gross motor, fine motor, cognition, language, social, and self-help [21,22]. For children over the age of 12 months, there are additional items that assess possible ASD symptoms, including eye contact, response to name, behavior for sharing interests like joint attention, severe delay in language, interests in peers, imaginative play and cooperative play, and children who do not exhibit these behaviors are recommended in-depth evaluation (Supplementary Table 2 in the online-only Data Supplement). However, referral rate to child psychiatrists is low, and studies that examine the clinical utility of K-DST in ASD screening are warranted [23].

DIAGNOSTIC EVALUATION

When ASD symptoms are discovered on a screening test, comprehensive diagnostic assessment should be performed. Clinicians should obtain the development history related to ASD symptoms, and assess social skills, communication skills and behavior through direct observation. Clinicians should consider using structured assessment tools to aid information collection. Diagnostic assessment should include a profile of the strengths, and weaknesses of the individual and should be conducted using an optimal approach by a multidisciplinary team with appropriate techniques and experience.

Diagnostic tools available in Korea include Autism Diagnostic Interview-Revised (ADI-R), Autism Diagnostic Observation Schedule 2 (ADOS-2), and the Childhood Autism Rating Scale, Second Edition (CARS-2). The ADI-R is a semi-structured interview tool [24], which assesses 4 domains including language/communication skills, interaction, restricted and repetitive behavior and interest, and age of onset. Completion time is 90−150 minutes [25]. ADOS-2 is a direct observational tool implemented by trained professionals, and assesses social interaction, nonverbal communication, repetitive behavior and interest, and play characteristics, by using play and conversation as an interaction tool [26]. There are 5 modules to ADOS-2, applied according to chronological age and expressive language level, and each takes 40−60 minutes to complete. CARS-2 is based on history taking and observation [27], and the standard version is usually applied to children below age 6 or those with low intelligence quotient (IQ), whereas the high-functioning version can be applied to children above age 6 or individuals with an IQ score higher than 80. These tools introduced above should be conducted by a trained professional, and administrators should receive proper training in order to achieve high reliability, but the level of expert, completion time and intensity of training differs across tools. Although these tools have high reliability, they cannot replace the clinician's final diagnosis. Combination of the above-mentioned observational and interview measures, rather than relying on a single source of information, leads to the most accurate diagnosis [28,29].

BIOLOGICAL MARKERS FOR DIAGNOSIS

There is no current biomarker that can be used to diagnose ASD. Hence, ASD diagnosis cannot be established based on blood tests or radiological tests. However, there may be an underlying organic cause for ASD, and biological tests may be needed for differential diagnosis. If clinically relevant, all ASD patients should consider the following tests; physical exams for neurological and dysmorphic features, chromosomal microarray, hearing test, tests to rule out ASD-related conditions (e.g., Tuberous sclerosis).

Genetic testing

Clinically significant genetic abnormalities are found in 15%−20% of children with developmental disorders. Genet-

ic disorders known to be associated with ASD are presented in Supplementary Table 3 (in the online-only Data Supplement). Genetic testing can 1) predict physical complications related to genetic disorders beforehand, 2) provide counseling on the anticipated risk of recurrence of the same disorder within the family, 3) provide psychological support to the family by explaining the cause of the disorder, and 4) prevent unnecessary additional tests through confirmatory diagnosis [9].

The American College of Medical Genetics and Genomics, American Academy of Child and Adolescent Psychiatry, and American Academy of Pediatrics recommend testing of copy number variants by chromosomal microarray for all developmental disorder patients with unknown genetic causes [14,30,31]. Genetic testing is especially necessary when a genetic syndrome is suspected by physical exam. For example, Fragile X syndrome patients may show a large head circumference, a prominent chin, large ears, ligamentous laxity and large testes. *PTEN* testing is recommended if the head circumference is more than 2.5 standard deviations above mean for age. *MECP2* testing is recommended for Rett syndrome in girls with severe intellectual disabilities, and karyotype analysis if a chromosomal syndrome is suspected [31]. A pedigree of three generations and physical examinations should be performed before genetic testing. There is no established consensus on genetic testing of ASD in South Korea yet.

Other organic tests

Brain magnetic resonance imaging (MRI) can be considered to identify structural, anatomical abnormalities or brain malformations. However, identification of causes that need treatment is rare, and routine examination is not recommended [32]. In those who show atypical regression, microcephaly or macrocephaly, seizure or epilepsy, evidence of brain structural abnormalities due to genetic syndromes, or abnormal signs on the neurologic exam; brain MRI may be considered [14].

Metabolic disorders to consider for differential diagnosis are presented in Supplementary Table 4 (in the online-only Data Supplement). However, as clinically meaningful findings are not common, routine exams are not recommended. In those with a history of atypical regression (e.g., motor regression after age 2 or multiple regression), family history of metabolic disorders, hypotonia or weakness, visual and hearing impairment, dysmorphic features in face or body, referral for evaluation of metabolic disorders may be warranted [33].

Although seizure risk is increased in ASD children, electroencephalogram (EEG) abnormalities not associated with clinical seizures are common. Routine EEG exams are not recommended, but those with suspected epilepsy, atypical regression like language loss in late ages, or neurological signs should be considered for EEG exams [34,35].

ASSESSMENT OF LANGUAGE, COGNITION, AND FUNCTIONING LEVEL

Evaluation of language, cognition, and overall functioning level should be included in ASD assessment. First, deficits in social communication can only be judged relative to what would be expected for someone's cognitive and language level. Therefore, this is especially critical for differential diagnosis as well as comorbid conditions (e.g., intellectual disability or language disorders). Accuracy of diagnosis is maximized based on comprehensive diagnostic assessment. Second, these functions determine the clinical manifestation of ASD symptoms and also the social and functioning level. Third, when establishing an interventional plan, functioning level must be considered. As all treatment and educational plans should be individualized according to the language, IQ, and cognitive function of the individual, the clinician must apprehend other functional characteristics besides ASD symptoms.

Cognitive function and IQ should be evaluated by a trained professional using age- and language-level-appropriate standardized tools that are available in each language and culture. Usually children aged 3 and higher can undergo standardized IQ tests, and children below this age should receive testing that measure developmental level. The Wechsler Scales of Intelligence, which include the Wechsler Preschool and Primary Scale of Intelligence (WPPSI), Wechsler Intelligence Scale for Children (WISC), and Wechsler Adult Intelligence Scale (WAIS), are the most commonly utilized tests of cognitive ability in evaluation of ASD [36]. In South Korea, the Psychoeducational Profile-Revised (PEP-R) is most widely used to evaluate language, motor development, and eye-hand coordination. The Bayley Scales of Infant and Toddler Development–Third Edition (Bayley-III) can assess cognition, receptive communication, expressive communication, fine motor development and gross motor development in infants and toddlers from 1 to 42 months old [37]. Nonverbal IQ tests can be applied in nonverbal children, and the K-Leiter-R [38] and Comprehensive Test of Nonverbal Intelligence Second Edition (K-CTONI-2) [39] have been standardized in Korean. Frontal lobe executive function tests should be administered in children with possible attention and executive function deficit.

The ability to comprehend, express language, and pragmatic skills should be assessed using standardized tools, according to the age, language level, and purpose of assessment. This will aid providing individualized training of communi-

cation skills to ASD children, and also help selection of the most appropriate ADOS module, and will act as a standard when diagnosing disabilities in social behavior in the context of the individual's language level. Assessment of adaptive skills is usually based on the report of parents or teachers, and obtaining information on self-help skills or daily living skills will help determining the goal of treatment. Although adaptive functioning is dependent on IQ levels, ASD individuals with normal IQ may have low adaptive functioning, and this may aggravate the degree of disability [40]. The Vineland Adaptive Behavior Scale-II [41] and Social Maturity Scale [42] is widely used in South Korea.

As ASD has a close relationship with visual and hearing disorders, and children with visual or hearing disorders may present symptoms similar to ASD, visual and hearing tests may be needed [43,44]. Those with delay in language development or prominent ADHD symptoms may require hearing tests, whereas those with visual inattention or stereotypies in which one places objects in front of their eyes may require visual tests.

DIAGNOSIS OF COMORBID CONDITIONS

ASD is a complex disorder, accompanied by various psychiatric, cognitive, neurological and medical disorders. Assessment and diagnosis of comorbid conditions is an important element of the ASD diagnosis process. First, comorbid conditions, regardless of ASD diagnosis, should be treated. Second, comorbid conditions not only affect the quality of life, but also can negatively influence the treatment effect of ASD. Certain psychiatric comorbidities respond well to cognitive-behavioral treatment or medication, so active assessment and early treatment are important. The diagnosis of psychiatric comorbidities of ASD should be conducted by a trained board-certified psychiatrist, and possible medical, neurological comorbidities should be referred to an appropriate professional.

The type and clinical importance of common comorbidities differ according to age, and the priority of assessment should be decided by developmental stage. Comorbidities requiring most clinical attention in preschool and early childhood are the genetic syndromes described above, neurological problems, communication disorders, and intellectual disability. Eating problems, sleeping disturbances, and motor control problems are also common at this age and require careful assessment and intervention. Common problems accompanied in childhood are attention deficit hyperactivity disorder (ADHD), oppositional defiant disorder, anxiety and obsessive compulsive disorder, and tic disorder [45,46]. Severe temper tantrums, aggression, anger, and self-harm can start in infancy and be accompanied at all ages.

Childhood-onset ADHD symptoms can continue into adolescence or the transitional period. Anxiety disorders and mood disorders like depression are warranted more clinical attention at this period [47,48]. ASD in adolescence and older ages may show atypical depressive symptoms, and suicidal ideation and behavior may appear [49]. In high-functioning ASDs, self-report may be more reliable than parent report in detecting depressive symptoms, so assessment methods should be selected according to the individual [50]. There may be problems that are inherent to ASD, but others may evolve as the result of interaction between individuals and their environment. A common example would be overweight, obesity, and metabolic syndromes that appear after adolescence [51].

Comorbidities that warrant clinical attention in ASD are presented in Supplementary Table 5 (in the online-only Data Supplement).

DIFFERENTIAL DIAGNOSIS

ASD generally requires differential diagnosis with developmental disorders including global developmental delay, intellectual disability, communication disorders, and ADHD, and also with brain developmental disorders with underlying organic causes. However, these disorders may also co-occur with ASD, so these disorders are not mutually exclusive. Instead of identifying ASD by ruling out other developmental disorders, first fulfillment of ASD diagnostic criteria. Differential diagnoses of ASD in adolescence or adulthood include avoidant and schizoid personality disorder, social anxiety disorder, chronic mood disorders like persistent depressive disorder, and schizophrenia. In these cases, it is necessary to evaluate whether social communication abilities or social relationships were impaired since childhood, and whether repetitive behaviors or fixed interests, sensory hypersensitivity were present during the developmental process.

SPECIAL CONSIDERATIONS IN DIAGNOSIS

Diagnosis in adults

Diagnosing ASD is more complex in adolescence, especially adults, and differential diagnosis may be challenging. The diagnostic process should be performed in a similar manner as in children, which is obtaining information on developmental history, whether current symptoms fulfill diagnostic criteria, and confirmation of comorbid symptoms. As evaluation of developmental history becomes more difficult as the individual grows older, records other than interviews

like the ADI-R, like past medical records, school records, and therapeutic records could be useful. According to the NICE guideline (2012), diagnosis of ASD in early adulthood should be considered in the following: 1) limited interactions with others, e.g., being aloof, indifferent, or unusual; 2) interaction to fulfill needs only; 3) naïve or one-sided interaction; 4) lack of responsiveness to others; 5) little or no change in behavior in response to different social situations; 6) limited social demonstration of empathy; 7) rigid routines and resistance to change; and 8) marked repetitive behaviors or activities.

Diagnosis in females

There has been consistent evidence suggesting that the prevalence of ASD in females has been underestimated. The possible explanation for this could be that the diagnostic criteria may not be sensitive or specific enough to identify ASD characteristics in women. ASD females without intellectual disability or behavior problems may not fulfill diagnostic criteria, possibly because they manifest a different phenotype with less "restrictive interests and repetitive behavior." The male-to-female ratio of ASD individuals with comorbid intellectual disability is 1:2. Considering that restricted interests and repetitive behavior are more common in intellectual disability, the adaptive and compensation abilities of ASD women with higher IQs may be the reason that women are less likely to surpass the ASD diagnostic threshold.

Research on how clinical expression differs between men and women have been contradictory. Commonly suggested findings are that ASD females compared to males 1) have a greater need to make friends and hang out with peers, 2) imitate peers and have less deficits in social play skills, 3) have better coping skills and are more likely to receive a provisional diagnosis at an older age compared to males with a similar level of ASD characteristics, 4) have less severe "repetitive and restricted behavior and interests" that do not manifest before age 6, 5) high prevalence of eating disorders, and 6) less impaired theory of mind [52,53]. However, a recent relatively large scale data [54] had suggested fairly minimal sex differences and that there may not be a need for female-specific diagnostic criteria or thresholds. Many studies are limited by ascertainment bias and thus more studies are needed to examine sex differences in manifestation of symptoms of ASD.

Delivering diagnosis

After confirmation of diagnosis and assessment of function and comorbidities, the process of delivering information about the diagnosis to the caregiver, and if necessary, to the individual is important. This is the first step in helping the family establish a short-term and long-term plan. Clinicians should use phrases that the family can understand, and provide clear explanation with precise medical terms. Clinicians should share information on the behavioral characteristics that were observed during the process of diagnosing ASD, the meaning of having a disorder, information on evidence-based intervention, and the anticipated disease course in the future, with an empathetic attitude. Clinicians should avoid reporting raw scores from diagnostic measures such as the ADOS and ADI-R as those scores do not represent the overall functioning of the individuals but focus on qualitative observations and descriptions that help the families understand their child's profiles. There is little research on how to deliver information on ASD diagnosis to the ASD individual after adolescence, but the clinician should discuss this process with the parents in advance, plan a follow-up visit to deal with the individual's response, and prepare for both positive and negative responses after delivery of diagnosis.

Supplementary Materials

The online-only Data Supplement is available with this article at https://doi.org/10.5765/jkacap.230009.

Availability of Data and Material

Data sharing not applicable to this article as no datasets were generated or analyzed during the study.

Conflicts of Interest

Hee Jeong Yoo, a contributing editor of the *Journal of the Korean Academy of Child and Adolescent Psychiatry*, was not involved in the editorial evaluation or decision to publish this article. All remaining authors have declared no conflicts of interest.

Author Contributions

Conceptualization: Johanna Inhyang Kim, Hee Jeong Yoo. Investigation: Johanna Inhyang Kim, Hee Jeong Yoo. Supervision: Hee Jeong Yoo. Writing—original draft: Johanna Inhyang Kim, Hee Jeong Yoo. Writing—review & editing: Johanna Inhyang Kim, Hee Jeong Yoo.

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