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Diagnostic assessment key in autism spectrum disorder

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What are the core symptoms?

How should children be assessed?

How should diagnosis be confirmed?

AUTISM SPECTRUM DISORDER (ASD) IS A COMPLEX PERVASIVE NEURODEVELOPMENTAL disorder with an estimated lifetime prevalence of 1%.[1] ASD presents across a wide range of intellectual ability and persists throughout life.

Core symptoms include abnormal social interaction and communication, restricted and repetitive interests or activities, associated with a lack of cognitive flexibility, and unusual sensory responses.[2]

DSM-5 designated ASD as a single diagnostic category incorporating a range of subtypes, including Asperger's syndrome. In addition, DSM-5 takes into account that the child's symptoms may not be recognised until social expectations increase later in life. DSM-5 has also created a new separate diagnostic category 'social communication disorder' for individuals who have social impairment in the absence of restricted/repetitive behaviour and sensory problems.

ICD-11 mirrors DSM-5 but differentiates autism with and without intellectual disability.[3] An overarching criterion for a diagnosis of ASD in both DSM-5 and ICD-11 is whether the observed symptoms are sufficiently severe to undermine the individual's functioning in everyday life.

'A child's symptoms may not be recognised until social expectations increase later in life'

ASD-related problems often require psychiatric input in their management, particularly as they are associated with a high frequency of co-occurring psychiatric disorders and clinical risk.

AETIOLOGY

Research evidence from genetic studies indicates that ASD is highly heritable.[4] A recent meta-analysis of twin studies found that the previously reported shared environmental influences are likely to be a statistical artefact arising from overinclusion of concordant dizygotic twins.[5]

However, the genetic risk for ASD is polygenic, often involving multiple single nucleotide polymorphisms, de novo mutations and copy number variations.[6] A population-based birth cohort study found that the risk of ASD is not limited to older paternal or maternal age alone but is also associated with increasing difference in age between the parents.[7] Molecular studies suggest that numerous genes may be involved, some of which may be epistatic.[8] A recent genome-wide association meta-analysis led to the identification of 93 significant genome-wide markers, of which 53 were replicated in independent cohorts.[9]

A strong propensity for ASD in males (male:female ratio 3:1) has been observed with striking consistency. It has been suggested that the gender difference in ASD prevalence may be caused by an increase in fetal testosterone. Baron-Cohen and colleagues hypothesise that fetuses exposed to high levels of testosterone are likely to develop ASD and that this condition can be considered an extreme of the normal male profile.[10]

Studies suggest that prenatal factors including maternal diabetes, (both pre-existing type 2 diabetes and gestational diabetes diagnosed ≤ 26 weeks), vitamin D deficiency, placental insufficiency and »

maternal obesity may play a crucial role in the aetiology of ASD.[11,12] A recent study found that children who were exposed to pre-eclampsia in utero were 32% more likely to develop ASD. A causal link between pre-eclampsia and ASD e.g. mediated by fetal hypoxia, oxidative stress or maternal systemic inflammation is plausible.[13] In addition, women who take antidepressants during the first trimester are almost twice as likely to give birth to children with ASD.[14]

Intrauterine exposure to infections such as cytomegalovirus and rubella are associated with increased risk of ASD.[15] Fetal alcohol syndrome caused by maternal drinking during pregnancy is often unrecognised but strongly associated with ASD.[16] Intrauterine exposure to several antiepileptic drugs, especially valproate, is also associated with an increased risk of ASD.[17] Perinatal factors have been examined indicating that low birthweight, breech and premature birth are associated with a raised risk of ASD.[18]

There is also an increased risk of ASD in children of mothers with thyroid dysfunction[19] and autoimmune disorders.[20] Autism is also linked to maternal/paternal schizophrenia, and maternal depression and personality disorders.[21]

However, a recent population-based birth cohort study across five countries including more than 2 million individuals followed up to the age of 16 years found that the heritability of ASD was approximately 80%, indicating that the variation in ASD occurrence in the population is mostly due to inherited genetic influences. There was little evidence to support the influence of maternal factors.[22]

PRESENTATION

GPs are often the first point of contact for parents or individuals seeking help for suspected ASD. The high rates of comorbidities, the wide-ranging levels of severity and symptom expression and recent changes to the diagnostic criteria make diagnosing ASD in primary care challenging.[23]

Although the behavioural presentation has a childhood onset, a large number of autistic adults may not have been formally diagnosed or may have been misdiagnosed with other psychiatric conditions. Many autistic children reach adulthood without being diagnosed. A study of children aged 5-9 years found that for every three known cases there were two undiagnosed cases.[24] Their symptoms may only come to the surface when they experience adversity in adult life, such as work-related stress, redundancy, divorce, bereavement or problems with the law. Presenting concerns are often about mental health rather than autism per se.

Psychiatric comorbidity is highly prevalent among individuals with ASD.[25] Depression, anxiety and attention deficit hyperactivity disorder (ADHD) are common in adults with ASD.[25] Around 20-22% of children and adults with ASD meet criteria for a tic disorder.[26] Compared with the general UK population, adults with Asperger's syndrome are much more likely to experience suicidal thoughts and plan or attempt suicide.[27]

Current evidence suggests autistic individuals have high rates of physical comorbidity, especially epilepsy, gastrointestinal disorders, metabolic syndrome and nutritional problems.[28]

Core symptoms of ASD may manifest differently according to gender, which may delay diagnosis in females. Girls with ASD are more likely to develop coping strategies to manage social situations that mask the degree of deficit.[29]

'Girls with ASD are more likely to develop coping strategies to manage social situations that mask the degree of deficit'

The signs listed in box 1, left, should make the clinician consider a referral to specialist services for a formal ASD assessment.

ASSESSMENT

NICE recommends that a multistage approach is used to identify children and young people at risk of ASD in primary care.[30] This should include:

- Eliciting and paying attention to parental concerns
- Observing speech delay, or regression, which is often the parents' first concern
- Reviewing the obstetric history for risk factors (low birthweight, prematurity, polyhydramnios, prenatal infections, multiple births, IVF, advanced maternal

Box 1

Signs warranting referral for a formal autism spectrum disorder assessment

Difficulties with social relationships:
- Few or no sustained relationships; those that exist are likely to be either distant or intense
- Persistent aloofness
- Awkward interaction with peers
- Unusually egocentric
- Little concern for others or awareness of their viewpoint
- Limited empathy or sensitivity
- Lack of awareness of social rules
- Problems in obtaining or sustaining education or employment

Abnormal communication:
- Odd or monotonous voice, often at an unusual volume
- One-sided conversation
- Stilted or pedantic language and difficulty understanding figurative speech
- Rather stilted, impassive appearance with limited gestures and rather odd or avoidant eye contact
- Awkward or odd posture and body language

Absorbing and narrow interests:
- Unusually circumscribed interests
- Obsessively pursued interests
- A set approach to everyday life that may include unusual routines or rituals
- Resistance to change

The behavioural presentation has a childhood onset

A known history of a neurodevelopmental condition, including learning disabilities and ADHD or other mental health disorder

key points

SELECTED BY

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Autism spectrum disorder (ASD) is a complex pervasive neurodevelopmental disorder with an estimated lifetime prevalence of 1%. ASD presents across a wide range of intellectual ability and persists throughout life. Core symptoms include abnormal social interaction and communication, restricted and repetitive interests or activities, associated with lack of cognitive flexibility, and unusual sensory responses. A key diagnostic criterion in both DSM-5 and ICD-11 is that symptoms must be sufficiently severe to undermine the individual's functioning in everyday life.

ASD is highly heritable and polygenic. The risk of ASD increases with advancing paternal and maternal age and is also associated with the parental age difference. The male: female ratio of ASD is 3:1. Antenatal risk factors include maternal diabetes (pre-existing and gestational), vitamin D deficiency, placental insufficiency, maternal obesity, and pre-eclampsia. ASD risk is also associated with intrauterine exposure to: infections such as cytomegalovirus and rubella; maternal drinking; antidepressants; and several antiepileptic drugs, especially valproate. Perinatal risk factors include low birthweight, breech delivery and premature birth.

Although the behavioural presentation has a childhood onset, approximately 40% of children with ASD are undiagnosed. In those who reach adulthood without being diagnosed, the symptoms may only come to the surface when they experience adversity, such as work-related stress, redundancy, divorce, bereavement or problems with the law. Presenting concerns are often about mental health rather than autism per se.

The following signs should make the clinician consider the possibility of ASD: difficulties with social relationships; abnormal communication; absorbing and narrow interests; onset in childhood; a known neurodevelopmental condition, including learning disabilities and ADHD. NICE recommends that GPs should: pay attention to parental concerns; recognise speech delay or regression; review the obstetric history for risk factors; and review the family history for developmental or psychiatric diagnoses. Developmental screening tools such as the Modified Checklist for Autism in Toddlers (M-CHAT) may be useful but should not be used to make or rule out a diagnosis of autism. If ASD is suspected based on screening or clinical judgement a referral to psychiatric services should be made.

Core symptoms in children can be improved by a social-communication intervention that uses play-based strategies with parents, carers and teachers to increase joint attention, engagement and reciprocal communication. Challenging behaviour should be addressed through the clear identification of target behaviours, assessment and modification of environmental factors that may contribute to initiating or maintaining the behaviour, and consistent application in all settings.

or paternal age, and less than 18 months between deliveries)
- Reviewing family history with heightened surveillance if there are siblings or close relatives with developmental or psychiatric diagnoses
- Standardised developmental screening such as the Modified Checklist for Autism in Toddlers (M-CHAT), a free validated tool that can be used in primary care (www.mchatscreen.com)
- Observing the child

A systematic review, however, found that the M-CHAT had moderate sensitivity and low specificity among children with developmental concerns. The authors concluded that it had limited value because of the high number of false positives.[31]

Screening tools should not be used exclusively to make or rule out a diagnosis of autism. If ASD is suspected based on screening or clinical judgement, a referral to psychiatric services should be made for diagnostic assessment.

'If ASD is suspected based on screening or clinical judgement a referral to psychiatric services should be made'

For those cases where diagnosis is less straightforward, or the clinical management is more complex because of comorbidity and clinical risk, there needs to be access to local specialist expertise and, where necessary, to tertiary specialist services. This applies particularly to the provision for psychiatric inpatient admission, as autistic individuals often find generic psychiatric wards very distressing.

Making a diagnosis of ASD is a lengthy multistage process. It requires multidisciplinary assessment of current symptoms, a detailed developmental history from a primary caregiver and the exclusion of alternative diagnoses by the psychiatrist.[32] The diagnostic process involves a direct clinical assessment of the individual and an interview with collateral informants, review of early health records, reports from school, assessment of cognitive skills and a medical examination.

In addition, the diagnostic process includes a detailed assessment of the following risk factors to outline a risk management plan:
- Self-harm
- Self-neglect
- Harm to others
- Breakdown of family or residential support
- Exploitation or abuse by others

Additional assessments are often carried out to aid the diagnostic process. These include:
- A formal IQ test to identify discrepancies between verbal and performance abilities as well as the variety of specific disabilities
- Assessment of functional ability to determine the extent to which there may be difficulties in everyday living skills, social relationships, communication, occupational and executive function, as well as identifying areas of talent that might be developed

MANAGEMENT

There is no robust evidence of any effective pharmacological treatment for the core symptoms of ASD.[33] The management of core symptoms in children and young people involves social-communication interventions that include play-based strategies with parents, carers and teachers to increase joint attention, engagement and reciprocal communication.[34] For example, interventions focusing on increasing children's interactive play with peers.

Strategies are adjusted to the child's developmental level and aim to increase the parents' or teachers' understanding of, and responsiveness to, the child's patterns of communication.

Applied behavioural analysis for children and young people with ASD has been shown to be effective and helps improve long-term outcomes.[35] Through reinforcement, new positive behaviour (such as learning to talk or acquiring social skills) is encouraged, and challenging behaviour is reduced.

Psychosocial interventions for challenging behaviour include clearly identified target behaviour, assessment and modification of environmental factors (e.g. sensory issues) that may contribute to initiating or maintaining the behaviour, and consistent application in all settings.[34]

It is imperative that children and young people with autism have full access to health and social care services, including mental health services, regardless of their intellectual ability.

Cognitive behaviour therapy has been reviewed by NICE,[32] but less attention has been given to other types of psychotherapy and counselling, because of the lack of adequate trials of these »

interventions in patients with ASD.

The functional difficulties associated with ASD, may be helped by a variety of non clinical resources outside the health service. These include peer group support through voluntary groups, social care and residential services, educational services (including higher and further education) providing support with developing social skills, stress management, preparation for work and accessing leisure activities.

Psychotropic drugs are often prescribed in this population to treat comorbid psychiatric disorders or manage associated symptom behaviours such as aggression, self-injury, hyperactivity, impulsivity and sleep problems. There is some evidence for the use of risperidone and aripiprazole in the management of repetitive behaviour,[33] but routine use is not recommended because of the potential side effects. If used, clinicians should monitor the clinical response closely and weigh up the risks and benefits.

A number of trials of SSRIs have been carried out but all have involved small selective samples and demonstrated mixed results.[33] A recent Cochrane review concluded that there is no evidence to support the use of SSRIs in children, whereas there are data to support their use in adults, specifically for repetitive behaviours.[36]

Oxytocin nasal spray has shown some encouraging preliminary results on social interaction deficits in children aged between 3 and 8 years of age,[37] although large scale randomised clinical trials are required. There are also promising results with the use of the glutamatergic drug riluzole for treating core symptoms of ASD.[38] However, few studies have examined riluzole as monotherapy and further research is required to ascertain its benefit in the treatment of ASD.

CONCLUSION

ASD is a complex neurodevelopmental disorder characterised by abnormalities in social communication and stereotyped repetitive behaviour. The aetiology of ASD is complex involving multiple genetic and environmental factors.

Individuals with autism may present to health services with co-occurring psychiatric disorders, and ASD may be overlooked if it is not considered during the assessment.

Many children with ASD reach adulthood before their condition is diagnosed, their symptoms coming to the surface only with experience of adversity. Screening instruments are useful but should not be used exclusively to make or rule out the diagnosis. If ASD is suspected based on screening or clinical judgement, a referral to psychiatric services should be made for comprehensive diagnostic assessment. The diagnostic process involves a direct clinical assessment of the individual and a detailed interview with collateral informants, assessment of cognitive and functional skills and a medical examination.

Competing interests: None

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