Clinical Neurogenetics

Autism Spectrum Disorders

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KEYWORDS

• Autism • Autism spectrum disorders • Genetic testing • Chromosomal microarray

KEY POINTS

- Autism spectrum disorders (ASDs) are defined by difficulties in social communication, language delay, and repetitive or restricted interests.
- The behavioral symptoms of ASDs manifest early in life and there are numerous screening tools to help clinicians identify patients.
- Although most cases of ASDs are idiopathic, there are syndromic forms of ASDs in which the behavioral deficits of autism are accompanied by other medical comorbidities.
- Chromosomal microarray testing is a recommended method for identifying syndromic forms of ASD and informing parents about potential medical problems as well as helping with family planning.

INTRODUCTION

Autism spectrum disorders (ASDs) are a prevalent disorder of childhood that affects an estimated 1 of 88 children in the United States.[1] Consequently, a wide range of medical practitioners, including pediatricians, pediatric neurologists, and child psychiatrists, are likely to encounter new cases. In this article, current recommendations concerning genetic testing in the routine evaluation of ASDs are summarized, a case study is presented to illustrate the utility of such a workup and what is currently known about the genetics and pathophysiology is reviewed.

ASD is an umbrella term defined by the Diagnostic and Statistical Manual (DSM-IV TR) that encompasses a range of disorders that have behavioral deficits in 3 core domains: social interaction, repetitive behaviors/restricted interests, and language.

Definition

- Patients with ASDs have deficits in 3 core domains:
  1. Social interaction
  2. Repetitive behavior/restricted interests

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3. Language

- Symptoms must be present before age 3. However, parent report of historical data before age 3 can be used to make the diagnosis later in life.
- Patients with deficits in all 3 domains significant enough to cause functional impairments have autistic disorder or autism
- Patients with deficits in social interaction and repetitive behavior/restricted interests but not language before age 2 have Asperger syndrome
- Patients with deficits in one or more domains that are significant enough to cause functional impairments but do not meet criteria for Autism or Asperger syndrome are diagnosed with pervasive developmental disorder not otherwise specified (PDD NOS)
- Some patients with ASDs may show a period of normal development before showing regression in motor, social, or cognitive skills
- Patients with Rett syndrome or childhood disintegrative disorder may meet criteria for autism, but more frequently only have deficits in 1 or 2 of the core domains or may develop these deficits after the age cutoff. For this reason, Rett and childhood disintegrative disorder are considered pervasive developmental disorders.

In next revision of the DSM (DSM-V), the definition of ASDs will be altered such that patients with autism, Asperger syndrome, and PDD NOS will all carry the diagnosis of ASD. These patients will be differentiated from each other with the use of modifiers to the ASD diagnosis, such as ASD with intact language and mild repetitive behavior or ASD with severe intellectual disability and language deficits. In addition, patients with deficits in social interaction and/or language but not repetitive behavior/restricted interests will receive a new diagnosis of social communication disorder.

SYMPTOMS AND CLINICAL COURSE

Patients with ASDs typically come in for an evaluation because of parental concern about a child's communication, lack of developmental milestones, or problematic behavior (tantrums, social conflict). Although there are research efforts to diagnose cases of ASDs in infancy,[2,3] current diagnostic tools are validated in toddlers and most children still do not receive a diagnosis until age 4 or later.[1] If left untreated, the behavioral deficits associated with ASDs do not improve with age. ASDs are a very clinically heterogeneous group of disorders with the behavioral deficits varying greatly from patient to patient. However, there are certain medical comorbidities that occur frequently enough with ASDs to be clinically relevant.

Medical comorbidities

- Sleep Disturbances

Parental surveys indicate that 50% to 80% of patients with ASDs have sleep problems, which may be treated with a combination of environmental modifications and medications.[4]

- Head Circumference

The rate of macrocephaly among patients with ASDs is between 17% and 20%, compared with 3% in the general population.[5,6] In addition, there is evidence that the rate of brain growth during the first year of life is greater in patients with ASDs compared with the general population.[7,8]

- Seizures

Seizures are more common in syndromic forms of ASDs (up to 60%) but can also occur in idiopathic ASDs at a rate of 5% to 10%.[9,10]