Autism spectrum disorders

Patricia Howlin

Abstract

This contribution presents an update on recent research into autism spectrum disorders (ASD). The areas covered include the genetic and neurological bases of ASD and the procedures required for accurate diagnostic assessment. Findings that challenge traditional views of ASD, particularly related to prevalence rates (now known to be much higher than originally believed), and levels of cognitive and linguistic ability are also discussed. The results of treatment trials are variable and the need for a much higher level of experimental sophistication in intervention research is highlighted. The necessity of providing more effective treatments and support networks for adults with ASD, rather than the focus being almost entirely on children, is stressed.

Keywords Asperger syndrome; autism; autism genetics; autism spectrum disorders; learning disability

What's new?

- Autism spectrum disorders are now known to affect as many as 6 children in every 1000
- Recent epidemiological studies suggest that the majority of children with autistic spectrum disorders have an IQ within the average range (i.e. 70+) and most acquire some useful speech
- Research to find the genes that may be implicated in autistic spectrum disorders continues. Although some potential loci have been identified, work in this area still has a long way to go and research into the interaction between genetic and environmental factors has barely begun
- Autistic spectrum disorders are highly complex and variable conditions and thus no single treatment is likely to be effective for all. Randomized control trials of different treatments are urgently needed, together with more systematic exploration of individual and external variables that moderate treatment effectiveness

Autism spectrum disorders (ASDs) comprise a group of conditions within the category of childhood-onset pervasive developmental disorders (PDD).[1,2] Other conditions within the PDD category include atypical autism and PDD-Not Otherwise Specified (PDD-NOS). Rett syndrome and childhood disintegrative disorder are also included in this category, although these latter have very different causes and trajectories. ASDs are characterized by abnormalities in three domains:

- reciprocal social interactions
- communication
- restricted and repetitive patterns of behaviour or interests.

Onset usually occurs in the first 3 years of life. The term 'spectrum' is used to indicate the wide range of abilities and difficulties associated with ASD. The two principal (and best defined) subgroups within the spectrum are childhood autism ('autistic disorder' in DSM-IV) and Asperger syndrome (see Tables 1 and 2).

Defining ASDs

The first descriptions of autism and Asperger syndrome appeared in the medical literature in the early 1940s. Most, but not all, of the cases described by Kanner showed marked delays in language and cognitive ability. Accounts by Asperger, in contrast, focused on relatively high-functioning individuals. Asperger syndrome was not widely recognized until the late 1980s, when Lorna Wing highlighted the fact that autistic disorders could also occur in individuals of high linguistic and cognitive ability. Current diagnostic criteria for Asperger syndrome are very similar to those for autism, but in Asperger syndrome there is no clinically significantly delay of language or cognitive development (see Table 1). There is considerable debate as to whether Asperger syndrome and autism should be classified as separate conditions, as is currently the case in DSM-IV and ICD-10. Most recent research indicates that if groups are matched appropriately for age and IQ, there are no qualitative differences between individuals with Asperger syndrome and high-functioning individuals with autism.[3]

Prevalence

Once considered to be a very rare disorder, occurring in only around 3 or 4 children per 10,000, recent epidemiological research indicates that the rate for autistic disorder is around 19 per 10,000; 9.5 per 10,000 for Asperger syndrome and 31 per 10,000 for PDD-NOS, giving a combined prevalence estimate for all PDDs of 60.6 per 10,000 (95% CI 51.6–70.7).[4] When consistent ascertainment methods have been used, there has been little change in prevalence rates in cohorts assessed between 1992 and 1998. This finding goes against claims of a current 'epidemic' of autism (see below) but rather suggests that recent increases in rates of diagnosis reflect greater awareness of autism spectrum disorders amongst professionals, together with widespread improvements in diagnostic practice.

Sex ratio: the overall male:female ratio is estimated at around 4 to 1 (similar to that for other language-related developmental disorders),

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ICD-10 criteria for autism

A Abnormal or impaired development is evident before the age of 3 years in at least one of the following areas:
- **1** receptive or expressive language as used in social communication
- **2** the development of selective social attachments or of reciprocal social interaction
- **3** functional or symbolic play.

B A total of at least six symptoms from within (1), (2) and (3) must be present, with at least two from (1) and at least one from each of (2) and (3):
- **1** Qualitative abnormalities in reciprocal social interaction are manifest in at least two of the following areas:
- **a** failure adequately to use eye-to-eye gaze, facial expression, body posture and gesture to regulate social interaction
- **b** failure to develop (in a manner appropriate to mental age, and despite ample opportunities) peer relationships that involve a mutual sharing of interests, activities and emotions
- **c** lack of socioeconomic reciprocity as shown by an impaired or deviant response to other people's emotions; or lack of modulation of behaviour according to social context; or a weak integration of social, emotional and communicative behaviours
- **d** lack of spontaneous seeking to share enjoyment, interests or achievements with other people (e.g. lack of showing, bringing or pointing out to other people objects of interest to the individual).

- **2** Qualitative abnormalities in communication are manifest in at least one of the following areas:
- **a** delay in, or total lack of, development of spoken language that is not accompanied by an attempt to compensate through the use of gesture or mime as an alternative mode of communication (often preceded by a lack of communicative babbling)
- **b** relative failure to initiate or sustain conversational interchange (at whatever level of language skills is present), in which there is reciprocal responsiveness to the communications of the other person
- **c** stereotyped and repetitive use of language or idiosyncratic use of words or phrases
- **d** lack of varied spontaneous make-believe or (when young) social imitative play.

- **3** Restricted, repetitive and stereotyped patterns of behaviour, interests and activities are manifest in at least one of the following areas:
- **a** an encompassing preoccupation with one or more stereotyped, restricted patterns of interest that are abnormal in content or focus; or one or more interests that are abnormal in their intensity and circumscribed nature though not in the content or focus
- **b** apparently compulsive adherence to specific, non-functional routines or rituals
- **c** stereotyped and repetitive motor mannerisms that involve either hand or finger flapping or twisting, or complex whole-body movements
- **d** preoccupations with part-objects or non-functional elements of play materials (such as their odour, the feel of their surface, or the noise or vibration that they generate).

Table 1

although amongst individuals with high IQ, including those with Asperger syndrome, the sex ratio may be closer to 10 to 1.

Causes

Genetics

Theories about causation have changed markedly over the years. In Kanner's time it was widely believed that the primary cause was inadequate parenting. Recent rises in prevalence estimates have resulted in claims that environmental factors such as vaccines (particularly mercury-based or MMR), pollutants, dietary additives, etc. are responsible. However, there is no evidence to support such claims and the cause is now considered to be predominantly genetic. There is an increased risk of autism in siblings of children with ASD and extremely high concordance rates amongst monozygotic twins. Family studies have identified higher rates of ASD-related problems (social-communication difficulties and/or circumscribed interests/stereotyped behaviours) amongst other relatives. These individuals are often described as falling within the 'broader autism phenotype'. The disorder is not inherited in a simple Mendelian fashion but the exact pattern of inherence is unclear. Current research focuses on the identification of susceptibility genes within specific chromosomal regions, particularly 7q22-q33 (notably the RELN and FOXP2 genes) and 15q11-q13 (in the area of the $GABA_A$receptor gene cluster). Other regions of interest include 2q, 13q, 16p and 19p.[5]

Neurobiology

Recent developments in brain imaging techniques allow for much more sophisticated investigation of the neurological deficits underlying ASD. Various abnormalities have been identified (e.g. in the fusiform gyrus, amygdala, cerebellum, cerebral cortex and in overall brain size). Post-mortem and neuroimaging studies also suggest that decreased functional connectivity may play a significant role. However, sample size in these studies is typically very small, diagnostic criteria are often unclear and the impact of variables such as age, intellectual impairment or language level is rarely assessed. A recent review stresses the need for larger scale and more rigorous research and concludes that functional imaging techniques need to be supplemented by other approaches (structural imaging, diffusion tensor imaging and electrophysiological techniques) in order to achieve an integrated model of the brain bases of ASDs.[6]

Neurochemistry

Research into the neurochemistry of ASD has also been limited by methodological shortcomings. There are few well replicated

