

Autism and Asperger syndrome: an overview

Autismo e síndrome de Asperger: uma visão geral

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Abstract

Autism and Asperger syndrome are diagnostic entities in a family of neurodevelopmental disorders disrupting fundamental processes of socialization, communication and learning, collectively known as pervasive developmental disorders. This group of conditions is among the most common developmental disorders, affecting 1 in every 200 or so individuals. They are also the most strongly genetically related among developmental disorders, with recurrence risks within sibships of the order of 2 to 15% if a broader definition of affectedness is adopted. Their early onset, symptom profile, and chronicity implicate fundamental biological mechanisms involved in social adaptation. Advances in their understanding are leading to a new social neuroscience perspective of normative socialization processes and specific disruptions thereof. These processes may lead to the emergence of the highly heterogeneous phenotypes associated with autism, the paradigmatic pervasive developmental disorder, and its variants. This overview focuses on the history, nosology, and the clinical and associated features of the two most well-known pervasive developmental disorders – autism and Asperger syndrome.

Keywords: Autism/therapy; Asperger syndrome/therapy; Psychopharmacology/standards; Child development/drug effects; Disease management

Resumo

Autismo e síndrome de Asperger são entidades diagnósticas em uma família de transtornos de neurodesenvolvimento nos quais ocorre uma ruptura nos processos fundamentais de socialização, comunicação e aprendizado. Esses transtornos são coletivamente conhecidos como transtornos invasivos de desenvolvimento. Esse grupo de condições está entre os transtornos de desenvolvimento mais comuns, afetando aproximadamente 1 em cada 200 indivíduos. Eles estão também entre os com maior carga genética entre os transtornos de desenvolvimento, com riscos de recorrência entre familiares da ordem de 2 a 15% se for adotada uma definição mais ampla de critério diagnóstico. Seu início precoce, perfil sintomático e cronicidade envolvem mecanismos biológicos fundamentais relacionados à adaptação social. Avanços em sua compreensão estão conduzindo a uma nova perspectiva da neurociência ao estudar os processos típicos de socialização e das interrupções específicas deles advindas. Esses processos podem levar à emergência de fenótipos altamente heterogêneos associados ao autismo, o paradigmático transtorno invasivo de desenvolvimento e suas variantes. Esta revisão foca o histórico, a nosologia e as características clínicas e associadas aos dois transtornos invasivos de desenvolvimento mais conhecidos – o autismo e a síndrome de Asperger.

Descritores: Autismo/terapia; Síndrome de Asperger/terapia; Psicofarmacologia/efeito de drogas; Desenvolvimento infantil/efeito de drogas; Gerenciamento da doença

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Introduction

Autism and Asperger syndrome are the best known among the pervasive developmental disorders (PDD), a family of conditions marked by early-onset delays and deviance in the development of social, communicative, and other skills. In the revised fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR), the PDD category includes conditions that are invariably associated with mental retardation (Rett's syndrome and Childhood Disintegrative Disorder), conditions that may or may not be associated with mental retardation (autism and PDD not otherwise specified or PDD-NOS), and one condition that is typically associated with normal intelligence (Asperger syndrome). The PDDs are among the most common developmental disorders. They refer to a family of conditions characterized by great variability of clinical presentations. They vary in terms of both profile of symptomatology and degree of affectedness but cluster together around the early-onset disruption of the socialization processes. They are neurodevelopmental in nature and have impact on basic and early-emerging brain mechanisms of sociability. Thus, they result in disruption of normal processes of social, cognitive, and communication development. Awareness of the heterogeneity of behavioral manifestations, of variable degrees of affectedness, and of likely multiple etiologic factors gave rise to the term Autism Spectrum Disorders, which, like the term PDD, refers to several discrete conditions (autism, Asperger syndrome, and PDD-NOS), but which, unlike the term PDD, refers to a postulated dimensional nature linking various conditions rather than clear-cut boundaries around diagnostic labels. This concept of a dimensional nature is supported by the fact that autism and related conditions are the most strongly genetically related developmental disorders, and by the fact that social vulnerabilities and rigidities may be found in relatives of these patients even when these relatives do not meet criteria for a clinical diagnosis. These relatives are often referred to as presenting the "broader autism phenotype".¹⁻²

This review focuses on the paradigm of PDD (autism), as well as on a close variant (Asperger syndrome). While the validity of autism diagnosis is unquestionable, the validity status of Asperger syndrome (AS) is still quite tentative, even 12 years after its formalization in DSM-IV. This uncertainty about diagnostic validity is particularly related to the fact that this diagnosis is confounded with autism unaccompanied by mental retardation, or "higher functioning" autism (HFA). We will emphasize the description of prototypical cases of these conditions. Nevertheless, current scientific discussions in this field tend to focus attention on potential mediators of syndrome expression (i.e., what predicts the differences in phenotypic presentation) rather than on differential diagnostic issues (i.e., the question whether HFA and AS are the same or different). A great deal of confusion still surrounds the usage of the term Asperger's syndrome or Asperger's disorder, with hardly any consensus among the community of clinical researchers.³ The emphasis of this review is not on research weighing one way or the other relative to the separation of AS and HFA. Rather it emphasizes the typical needs and challenges faced by individuals with these conditions regardless of the specific label assigned to them.

Autism

Autism, also known as *autistic disorder*, *childhood autism*, *infantile autism*, and *early infantile autism*, is the best known of the PDDs. In this condition, there is marked and sustained impairment in social interaction, deviance in communication, and restricted or stereotyped patterns of behaviors and interests. Abnormalities in functioning in each of these areas must be present by age 3. Approximately 60 to 70% of individuals with autism function in the mentally retarded range, although this percentage has been shrinking in more recent prevalence studies. This shrinking likely reflects increased awareness of higher functioning manifestations of autism, which, in turn, seems to lead to a larger number of individuals being diagnosed with this condition.⁴

1. History and nosology

In 1943, Leo Kanner first described 11 cases of what he termed *autistic disturbances of affective contact*.⁵ In these first 11 cases there was an "inability to relate" in usual ways to people since the beginning of life. Kanner also noted unusual responses to the environment, which included stereotyped motor mannerisms, resistance to change or insistence on sameness, as well as unusual aspects of the child's communication skills such as pronoun reversal and tendency to echo language (echolalia). Kanner was careful to provide a developmental context for his observations. He emphasized the centrality of deficits in social relatedness, as well as unusual behaviors in the definition of the condition. During the 1950's and 1960's, there was much confusion about the nature of autism and its etiology, with the most common belief being that autism was caused by parents who were emotionally unresponsive to their children (the "refrigerator mothers" hypothesis). In most of the world, such notions are all abandoned now, although they can still be found in parts of Europe and in Latin America. In the early 1960's, a growing body of evidence began to accumulate suggesting that autism was a brain disorder, present from infancy, and found in all countries, social economic and ethnic/racial groups in which researchers sought it. A landmark in classification occurred in 1978 when Michael Rutter proposed a definition of autism based on 4 criteria: 1) social delay and deviance not just a function of mental retardation; 2) communication problems, again, not just a function of associated mental retardation; 3) unusual behaviors, such as stereotyped movements and mannerisms; and 4) onset before age 30 months.⁶

Rutter's definition and the growing body of work on autism were influential in the definition of the condition in DSM-III in 1980, which is when autism was first recognized and placed in a new class of disorders, namely the pervasive developmental disorders (PDDs). The term PDD was chosen to reflect the fact that multiple areas of functioning are affected in autism and related conditions. By the time of DSM-III-R, the term PDD had taken root, leading to its adoption also in the tenth revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10). For DSM-IV, potential new criteria for autism, as well as several conditions that were candidates for inclusion under the PDD category, were evaluated in an international, multisite study including over 1,000 ca-

ses evaluated by more than 100 clinician raters.⁷ DSM-IV and ICD-10 classification systems were made equivalent to avoid potential confusion among clinical researchers working in different parts of the world guided by one or the other nosological system. Criteria definition was decided on the basis of empirical data revealed in the field trial. Inter-rater reliability was assessed for autism and related conditions, indicating generally good to excellent agreement among, particularly, experienced clinicians. The DSM-IV-TR provides updated accompanying text for autism, Asperger syndrome, and other PDDs, although the defining criteria themselves remained the same as in DSM-IV.

2. Epidemiology

The first epidemiological study of autism was conducted by Victor Lotter in 1966. In this study he reported a prevalence rate of 4.5 in 10,000 children among the entire 8- to 10-year old population of Middlesex, a county northwest of London. Since then, over 20 epidemiological studies have been reported in the literature surveying millions of children worldwide. Resulting prevalence rates, particularly in more recent studies, point to a conservative rate of 1 individual with (prototypical) autism per 1,000 births, and some additional 4 individuals with autism spectrum disorders (e.g., Asperger syndrome, PDD-NOS) per 1,000 births, and much smaller rates for Rett's syndrome, and much smaller still for childhood disintegrative disorder. Possible reasons for the great increase in prevalence estimative of autism and related conditions are: 1) the adoption of broader definitions of autism (as a result of recognition of autism as a spectrum of conditions); 2) greater awareness among clinicians and the larger community of the different manifestations of autism (e.g., thanks to more frequent media coverage); 3) better detection of cases without mental retardation (e.g., more awareness of HFA and AS); 4) the incentive to attain a diagnosis given the eligibility for services conferred by this diagnosis (e.g., in the US, as a result of changes in special education law); 5) the understanding that early identification (and intervention) maximize a positive outcome (thus encouraging the diagnosis of young children, and encouraging the community not to "miss" a child with autism, who otherwise would not get needed services); and 6) population-based screening (which expanded self-referred clinical samples by systematically "combing" the community at large for children with autism who otherwise might not be identified as such). It is important to emphasize that increase in prevalence rates of autism mean that more individuals are identified as having this and similar conditions. It does not mean that the general incidence of autism is increasing. The latter belief has led to the notion of a possible "epidemic" of autism (i.e., that the number of individuals with autism is increasing in alarming numbers). To date, there is no convincing evidence that this is true, and potential environment hazards hypothesized to be "triggers" of such an epidemic (e.g., vaccination programs) have not received any empirical validation in multiple, large-scale studies conducted in Scandinavia, Japan, and the US, among others.⁸ Unfortunately, the belief among some is still strong that vaccination (e.g., the MMR or measles/mumps/rubella

vaccine), or that preservatives used in immunization programs (e.g., thimerosal) may cause autism. This belief has prompted many parents to withdraw their children from immunization programs. As result, data are accumulating in the UK and US suggesting the dangerous reappearance of these serious diseases, particularly measles that can lead to mental retardation or even death.

One interesting finding involving both clinical and epidemiological samples is that there is a higher incidence of autism in boys than in girls, with ratios reported averaging around 3.5 or 4.0 males to 1 female. This ratio varies, however, as a function of intellectual functioning. Some studies have reported ratios of up to 6.0 or more males to each female in individuals with autism without mental retardation, whereas ratios within the moderately to severely mentally retarded range have been reported to be as low as 1.5 to 1. It is still unclear why females are under represented in the non-retarded range. One possibility is that males have a lower threshold for brain dysfunction than females, or, conversely, that more severe brain damage would be required to cause autism in a girl. According to this hypothesis, when the person with autism is a girl, she would more likely to be severely cognitively impaired. Several other hypotheses have been proposed, including the possibility that autism is an x-linked genetic condition (thus making males more vulnerable), however data are still limited for making possible any conclusions at present.

3. Diagnosis and clinical features

A diagnosis of autistic disorder requires at least six behavioral criteria, one from each of the three clusters of disturbance in social interaction, communication and restricted patterns of behavior and interest.⁹ There are 4 defining criteria in the cluster "Qualitative impairment in social interactions", including marked impairment in the use of nonverbal forms of communication and social engagement; failure to develop peer relationships; a lack of behaviors indicating sharing of experiences and shared communication (e.g., "joint attention" skills – showing, bringing, or pointing out objects of interest to other people); and lack of social or emotional reciprocity. The 4 defining criteria for "Qualitative impairment in communication" include delays in the development of spoken language not accompanied by an attempt to compensate through alternative modes of communication such as gestures in nonverbal individuals; impairment in the ability to initiate or sustain a conversation with others (in speaking individuals); stereotyped and repetitive use of language; and lack of spontaneous make-believe or social imitative play (in excess of what would be expected from the child's overall cognitive level). The 4 criteria in the cluster "Restricted repetitive and stereotyped patterns of behavior, interests, and activities" include encompassing, intense, and rigid preoccupations with stereotyped and restricted patterns of interest; inflexible adherence to specific nonfunctional routines or rituals; stereotyped and repetitive motor mannerisms (such as hand or finger flapping, whole body rocking); and persistent preoccupation with parts of objects (e.g., the texture of a toy, the wheels of a miniature car). As noted, the diagnosis of autistic disorder also requires abnormal development in at

least one of the following: social, language and communication, or symbolic/imaginative play in the first 3 years of life. And if the child meets criteria for Rett's syndrome or childhood disintegrative disorder, these disorders take precedence over autism.

There is a marked range of syndrome expression in autism. Among the lowest functioning children, the child typically is largely or entirely mute, is isolated from social interaction and makes few social overtures. At the next level the child may accept social interaction passively but does not seek it out. At this level, some spontaneous language may be observed. Among the higher functioning and somewhat older individuals, the child's social style is different in that he or she may be interested in social interaction but cannot initiate it or sustain it in typical ways. The social style of such individuals has been termed "active but odd" in that they often have difficulty regulating social interaction once it has commenced. Behavioral features of autism change over the course of development. There is considerable potential for misdiagnosis, especially at the extremes of levels of intellectual functioning. Evaluation of the child with autism should include a detailed history, comprehensive developmental, psychological, and communication assessments, and measurement of adaptive skills (i.e., abilities displayed spontaneously and consistently to meet the demands of everyday life). Additional examination may be required to rule out hearing impairment, and gross and fine motor as well sensory deficits or abnormalities. Medical examination should rule out seizures and tuberous sclerosis (see below in associated medical conditions), and genetic screening should rule out fragile X syndrome.¹⁰

1) Age at onset

The onset of autism is always before three years. Parents are typically concerned between the ages of 12 and 18 months as language fails to develop. Although parents may be concerned that the child does not hear (because of lack of response to verbal approaches), they also typically note that the child may respond quite dramatically to sounds in the inanimate environment (e.g., a vacuum cleaner, candy being unwrapped); occasionally parents report in retrospect that the child was "too good", made few demands and had little interest in social interaction. This is in stark contrast to typically developing infants for whom the human voice and face and social interaction are among the most interesting and salient features of the world. Occasionally parents report that the child seemed to develop some language, and then speech either plateaued or was lost; such a history is reported in about 20 to 25% of cases.¹¹ Almost always parents report being worried by age 2 and inevitably by age 3. With greater awareness of autism and its early signs (e.g., lack of eye contact, pointing, giving, or showing behaviors, or shared social joy), an increasing number of parents have concerns toward the end of the first year of life. Clearly, this sensitivity to delays and deviance in social development is heightened in families where an older sibling has already been diagnosed with autism. Occasionally, for very high functioning children with autism, parents may be less concerned in the first year or two of life, particularly if speech and language are emerging, but

even in these cases parents become concerned before the age of 3 as the severe deficits in social interaction become more apparent in situations other than in immediate contact with parents (e.g., in public places, in interaction with same age peers or relatives).

2) Qualitative impairments in social interaction

Normally developing infants have a marked interest in social interaction and the social environment from birth. Basic mechanisms of socialization such as selective attention to a smiling face or to highly intonated voices and playful movement prompt children to seek caregivers. The mutually reinforcing social choreography between infant and caregiver launches the development of social cognitive, communication, and symbolic skills. In infants and young children with autism the human face holds little interest; disturbances are seen in the development of joint attention, attachment, and other aspects of social interaction. For example, the child may not engage in the usual imitative games of infancy (e.g., peek-a-boo), may spent an inordinate amount of time exploring the inanimate environment when hearing incidental speech produced by others in the proximity. Play skills beyond sensory exploration of toys may be entirely missing. These deficits are highly distinctive and are not just due to associated developmental delay.¹²⁻¹³

Social interest may increase over time. There is often a developmental progression with younger and more impaired individuals being avoidant or aloof from interaction while somewhat older or more advanced individuals willing to passively accept interaction but not seeking it out. Among the most able persons with autism there is often social interest but the person has difficulty in managing the complexities of social interaction; this often leads to an unusual or eccentric appearing social style.

3) Qualitative impairment in verbal and nonverbal communication and play

As many as 20 to 30% of individuals with autism never speak. This percentage is considerably smaller now than it was some 10 to 15 years ago thanks in great part to early and intensive intervention. Delays in the acquisition of language are the most frequent presenting complaint of parents. Usual patterns of language acquisition (e.g., playing with sounds and babbling) may be absent or infrequent. Infants and young children with autism may guide the parent's hand to obtain a desired object without making eye contact (i.e., as if the hand, rather than the person, is obtaining the item). In contrast to the child with language disorder there is no apparent motivation to engage in communication or attempt to communicate via nonverbal means.

When individuals with autism do speak their language is remarkable in various ways. They may echo what is said to them (immediate echolalia), or what they hear in their environment, such as TV (delayed echolalia). Speech tends to be less flexible so that, for example, there is no appreciation that change in perspective or speaker requires pronoun change; this leads to pronoun reversal. Speech may be nonreciprocal in nature, e.g., the child produces language that is not meant as communication. While the syntax and morphology of language are relatively spared, vocabulary and semantic skills may be slow to develop and aspects of the

social uses of language (pragmatics) are particularly difficult for individuals with autism. Thus humor and sarcasm may be the source of confusion as the person with autism may fail to appreciate the speaker's communicative intent, resulting in an overly literal interpretation of the utterance. Often intonation of voice is flat or monotonic, and other communicative aspects of voice (e.g., stress, pitch, volume, and rhythm or phrasing) are idiosyncratic and poorly modulated.

Deficits in play may include a failure to develop the usual patterns of role-play, or make-believe, symbolic or imaginative play. The autistic child may explore nonfunctional aspects of play materials (e.g., taste or smell) or use aspects of materials for self-stimulation (spinning the tires on a toy truck).

4) Markedly restricted repertoire of activities and interests

Children with autism often have difficulty in tolerating change and variation in routine. For example, an attempt to alter the sequence of some activity may be met with catastrophic distress on the part of the child. Parents may report that the child insists that they engage in activities in very particular ways. Changes in routine or in the environment may elicit great opposition or upset. The child may develop an interest in a repetitive activity, e.g., collecting strings and using them for self-stimulation, memorizing numbers, repeating certain words or phrases. In younger children attachments to objects, when they occur, differ from usual transitional objects in that the objects chosen tend to be hard, rather than soft, and often it is the class of object, rather than the particular object, that is important, e.g., the child may insist on carrying a certain kind of magazine around with him or her. Stereotyped movements may include toe walking, finger flicking, body rocking, and other mannerisms; these are engaged in as a source of pleasure or self-soothing, and they may at times be exacerbated in situations of stress. The child may be preoccupied with spinning objects, e.g., he or she may spend long periods of time watching a ceiling fan rotate.

5) Associated features

As noted, 60 to 70% of individuals with autism have mental retardation, with about half of them falling within the mildly mentally retarded range and the remaining falling within the moderate to profound mental retardation range. It is well established that mental retardation is not simply a consequence of negativism or lack of motivation. The typical profile on psychological testing is marked by significant deficits in abstract reasoning, verbal concept formation and integration skills, and on tasks requiring a degree of verbal reasoning and social understanding.¹⁴ Therefore, on the Wechsler scales, for example, weaknesses are usually obtained on the Similarities and Comprehension subtests. In contrast, relative strengths are usually observed in the areas of rote learning and memory skills and visual-spatial problem solving, particularly if the task can be completed "piece meal", i.e., without having to infer the context or "Gestalt" of the task. Therefore, performance on the Block Design and Digit Recall subtests of the Wechsler scales usually correspond to the best performances. The typical preference for rote and sequential, rather than reasoning and integrative tasks, usually carry the implication that individuals with autism exhibit a very fragmented style of learning, failing to put different parts of a task, communication, or situations

into coherent wholes (as it were, failing to see "the trees from the leaves").¹⁵ Given the ubiquity of verbal deficits in autism, performance on the Wechsler scales is usually characterized by higher performance than verbal scores, particularly in the individuals scoring in the mentally retarded range. Higher functioning individuals with autism may show no verbal-performance IQ differential though still showing a preference for the rote tasks, verbal memory, and parts-to-whole visual reconstruction tests over conceptual and social reasoning tasks. "Executive" functions are often impaired, resulting in difficulty in planning, maintaining a goal in mind while executing steps to execute it, learning from feedback, and inhibiting irrelevant or inefficient responses.¹⁶

One of the most fascinating cognitive phenomena in autism is the presence of so-called "islets of special abilities" or splinter skills, i.e., preserved or very highly developed skills in specific areas which contrast with the child's overall deficits in cognitive functioning.¹⁷ It is not unusual, for example, for children with autism to have great facility in decoding letters and numbers, at times precociously (hyperlexia) even though comprehension of what is read is much impaired. Perhaps 10% of individuals with autism exhibit a form of "savant" skills – i.e., high, sometimes prodigious performance on a specific skill in the presence of mild or moderate mental retardation. This fascinating phenomenon usually relates to a narrow range of capacities – memorizing lists or trivial information, calendar calculation, visual-spatial skills such as drawing, or musical skills involving a perfect pitch or playing a piece of music after hearing it only once. Interestingly individuals represent a disproportionate majority of all "savant" persons.

Both hyper- and hypo-sensitivity to sensory stimuli are typical of children with autism. Children with autism may be acutely sensitive to sounds (hyperacusis), e.g., covering their ears when hearing a dog bark or the noise of a vacuum cleaner. Other children may appear oblivious to loud noise or people calling them, but may be fascinated by the faint ticking of a wristwatch or the sound of crumpling paper. Bright lights may be distressing, although some children are fascinated with light stimulation, e.g., moving an object back and forth in front of eyes. There may be extreme sensitivity to touch (tactile defensiveness), including major reactions to specific fabrics or social/affectional touch, while there are many children who appear insensitive to pain and may not cry after a severe injury. Many children are fascinated by certain sensory stimuli, such as spinning objects or toy parts that can spin, while some enjoy vestibular sensations such as twirling, engaging in this action without, apparently, becoming dizzy.

Sleeping and eating disturbances can be very taxing on family life, particularly during childhood. Children with autism may display erratic sleep patterns with recurrent awakening at night for long periods. Eating disturbances may involve aversion to certain foods because of their texture, color, or smell, or insistence on eating a very limited choice of foods and refusal to try new foods. In the more severely cognitively impaired children, pica (i.e., eating non-edible things) may pose a range of safety issues including the risk of lead toxicity.

Lower functioning children with autism may bite their hands or wrists, often leading to bleeding and callous formation.

Head banging, particularly in severely or profoundly mentally retarded, may necessitate the use of helmets or other protective devices. Children may also pick the skin, pull the hair, bang their chests, or hit themselves. There is a decreased sense of danger, which along with impulsivity, may lead to injuries. Temper tantrums are common, particularly in reaction to demands placed (e.g., to comply with a task), changes in routine or otherwise unexpected events. Lack of understanding or inability to communicate, or sheer frustration may occasionally prompt aggressive outbursts. Although some higher functioning individuals – e.g., those with Asperger syndrome – have been described as particularly vulnerable to exhibiting anti-social behaviors, it is in fact more likely that these individuals are victims of practical jokes or other forms of aggression; more commonly still, these individuals tend to gravitate toward the periphery of social settings.

4. Course and prognosis

Autism is a life-long disability, with the majority of individuals affected with this condition remaining unable to live independently, and requiring family, community support, or institutionalization. However, most children with autism show improvement in social relatedness, communication, and self-help skills with increasing age. Several factors are thought to be predictors of course and long-term outcome, particularly the presence of some communicative speech by the age of 5 or 6, nonverbal intellectual level, severity of the condition, and response to educational intervention. Younger children more typically display the “pervasive” unrelatedness typically included in earlier diagnostic systems. Although some evidence of differentiated responsiveness to parents may be observed as the child reaches elementary school, patterns of social interaction remain quite deviant. That notwithstanding, gains in social compliance and communication are often made during elementary school years, particularly if structured, individualized and intensive interventions are in place. During adolescence, some autistic children may exhibit behavioral deterioration; for a minority among these, the decline in language and social skills may be associated with the onset of a seizure disorder. Various interactional styles can be observed, ranging from aloof to passive, to eccentric (e.g., children who make attempts to initiate contact with others, but do so in a very awkward or rigid fashion); these styles are related to developmental level. Depressive and anxiety symptoms may appear in higher functioning adolescents, who become painfully aware of their inability to form friendships despite a desire to do so, and who begin to suffer the cumulative effect of years of failed contact with others, and teasing by peers.

Several long-term outcome studies¹⁸ suggest that approximately two thirds of autistic children have a poor outcome (unable to live independently), with perhaps only one third able to achieve some degree of personal independence and self-sufficiency as adults; among these, the majority may have a fair outcome (social, educational or vocational gains despite behavioral and other difficulties), whereas a minority (about a tenth of all individuals with autism) may have a good outcome (have a successful work placement and independent living).

Asperger syndrome

Asperger syndrome (AS) is characterized by impairments in social interaction and restricted interests and behaviors as seen in autism, but its early developmental course is marked by a lack of any clinically significant delay in spoken or receptive language, cognitive development, self-help skills, and curiosity about the environment. All-absorbing and intense circumscribed interests and one-sided verbosity as well motor clumsiness are typical of the condition, but are not required for diagnosis.

1. History and nosology

In 1944, Hans Asperger, an Austrian pediatrician with interest in special education, described four children who had difficulty integrating socially into groups.¹⁹ Unaware of Kanner's description of early infantile autism published just the year before, Asperger called the condition he described “autistic psychopathy”, indicating a stable personality disorder marked by social isolation. Despite preserved intellectual skills, the children showed marked paucity of nonverbal communication involving both gestures and affective tone of voice, poor empathy and a tendency to intellectualize emotions, an inclination to engage in long winded, one-sided, and sometimes incoherent speech, rather formalistic speech (he called them “little professors”), all-absorbing interests involving unusual topics which dominated their conversation, and motoric clumsiness. Unlike Kanner's patients, these children were not as withdrawn or aloof; they also developed, sometimes precociously, highly grammatical speech, and could not in fact be diagnosed in the first years of life. Discarding the possibility of a psychogenic origin, Asperger highlighted the familial nature of the condition, and even hypothesized that the personality traits were primarily male transmitted. Asperger's work, originally published in German, became widely known to the English speaking world only in 1981, when Lorna Wing published a series of cases showing similar symptoms.²⁰ Her codification of the syndrome, however, blurred somewhat the differences between Kanner's and Asperger's descriptions, as she included a small number of girls and mildly mentally retarded children, as well as some children who had presented with some language delays in their first years of life. Since then, several studies have attempted to validate AS as distinct from autism without mental retardation, although comparability of findings has been difficult due to the lack of consensual diagnostic criteria for the condition.³

AS was not accorded official recognition before the publication of ICD-10 and DSM-IV, although it was first reported in the German literature in 1944. Asperger's work was known primarily in German speaking countries, and it was only in the 1970's that the first comparisons with Kanner's work were made, primarily by Dutch researchers such as Van Krevelen, who were familiar with both English and German literatures. The initial attempts at comparing the two conditions were difficult because of major differences in the patients described – Kanner's patients were both younger and more cognitively impaired. Also, Asperger's conceptualization was influenced by accounts of schizophrenia and personality disorders, whereas Kanner had been influenced by the work of Arnold

Gesell and his developmental approach. Attempts at codifying Asperger's prose into a categorical definition for the condition were made by several influential researchers in Europe and North America, but no consensual definition emerged until the advent of ICD-10. And given the reduced empirical validation of the ICD-10 and DSM-IV criteria, the definition of the condition is likely to change as new and more rigorous studies emerge in the near future.²¹

2. Epidemiology

Given the lack of consensual definitions of diagnosis until recently, it is not surprising that the prevalence of the condition is unknown, although a rate of 2 to 4 in 10,000 has been reported.²² There is little doubt that the condition is more prevalent in males than females, with a reported ratio of 9 to 1. In the past few years, there have been a proliferation of parent support organizations organized around the concept of AS, and there are indications that this diagnosis is being given by clinicians much more frequently than even just a few years ago; there are also indications that AS is currently functioning as a residual diagnosis given to normal-intelligence children with a degree of social disabilities who do not fulfill criteria for autism, overlapping in this way, with the DSM-IV term PDD-NOS. Possibly the most common usage of the term AS is as synonymous or a replacement to autism in individuals with normative or superior IQs. This pattern has diluted the concept and reduced its clinical utility. Empirical validation of specific diagnostic criteria is badly needed, although this will have to await reports of rigorous studies employing standard diagnostic procedures, and validators truly independent of the diagnostic definition such as neuropsychological, neurobiological and genetic data.³

3. Diagnosis and clinical features

The diagnosis of AS requires the demonstration of qualitative impairments in social interaction and restricted patterns of interest, criteria which are identical to autism. In contrast to autism, there are no criteria in the cluster of language and communication symptoms, and onset criteria differ in that there should be no clinically significant delay in language acquisition, cognitive and self-help skills. Those symptoms result in significant impairment in social and occupational functioning.⁹

In some contrast to the social presentation in autism, individuals with AS find themselves socially isolated but are not usually withdrawn in the presence of others. Typically, they approach others but in an inappropriate or eccentric fashion. For example, they may engage the interlocutor, usually an adult, in one-sided conversation characterized by long-winded, pedantic speech, about a favorite and often unusual and narrow topic. They may express interest in friendships and in meeting people, but their wishes are invariably thwarted by their awkward approaches and insensitivity to the other person's feelings, intentions, and nonliteral and implied communications (e.g., signs of boredom, haste to leave, and need for privacy). Chronically frustrated by their repeated failures to engage others and form friendships, some individuals with AS develop symptoms of an anxiety or mood disorder that may require treatment, including medication.

They also may react inappropriately to, or fail to interpret the valence of the context of the affective interaction, often conveying a sense of insensitivity, formality, or disregard to the other person's emotional expressions. They may be able to describe correctly, in a cognitive and often formalistic fashion, other people's emotions, expected intentions and social conventions; yet, they are unable to act upon this knowledge in an intuitive and spontaneous fashion, thus losing the tempo of the interaction. Their poor intuition and lack of spontaneous adaptation are accompanied by marked reliance on formalistic rules of behavior and rigid social conventions. This presentation is largely responsible for the impression of social naiveté and behavioral rigidity that is so forcefully conveyed by these individuals.

Although significant abnormalities of speech are not typical of individuals with AS, there are at least three aspects of these individuals' communication patterns that are of clinical interest.²¹ First, speech may be marked by poor prosody, although inflection and intonation may not be as rigid and monotonic as in autism. They often exhibit a constricted range of intonation patterns that is used with little regard to the communicative functioning of the utterance (e.g., assertions of fact, humorous remarks). Rate of speech may be unusual (e.g., too fast) or may lack in fluency (e.g., jerky speech), and there is often poor modulation of volume (e.g., voice is too loud despite physical proximity to the conversational partner). The latter feature may be particularly noticeable in the context of a lack of adjustment to the given social setting (e.g., in a library, in a noisy crowd). Second, speech may often be tangential and circumstantial, conveying a sense of looseness of associations and incoherence. Even though in a very small number of cases this symptom may be an indicator of a possible thought disorder, the lack of contingency in speech is a result of the one-sided, egocentric conversational style (e.g., unrelenting monologues about the names, codes, and attributes of innumerable TV stations in the country), failure to provide the background for comments and to clearly demarcate changes in topic, and failure to suppress the vocal output accompanying internal thoughts. Third, the communication style of individuals with AS is often characterized by marked verbosity. The child or adult may talk incessantly, usually about a favorite subject, often in complete disregard to whether the listener might be interested, engaged, or attempting to interject a comment, or change the subject of conversation. Despite such long-winded monologues, the individual may never come to a point or conclusion. Attempts by the interlocutor to elaborate on issues of content or logic, or to shift the interchange to related topics, are often unsuccessful.

Individuals with AS typically amass a large amount of factual information about a topic in a very intense fashion. The actual topic may change from time to time, but often dominates the content of social interchange. Frequently the entire family may be immersed in the subject for long periods of time. This behavior is peculiar in the sense that oftentimes extraordinary amounts of factual information are learned about very circumscribed topics (e.g., snakes, names of stars, TV guides, deep fat fryers, weather information, personal information on

members of congress) without a genuine understanding of the broader phenomena involved. This symptom may not always be easily recognized in childhood since strong interests in certain topics, such as dinosaurs or fashionable fictional characters, are so ubiquitous. However, in both younger and older children typically the special interests become more unusual and narrowly focused.

Individuals with AS may have a history of delayed acquisition of motor skills such as pedaling a bike, catching a ball, opening jars, and climbing outdoor play equipment. They are often visibly awkward and poorly coordinated and may exhibit stilted or bouncy gait patterns and odd posture. Neuropsychologically, there is often a pattern of relative strengths in auditory and verbal skills and rote learning, and significant deficits in visual-motor and visual-perceptual skills and conceptual learning. Many children exhibit high levels of activity in early childhood, and, as noted, may develop anxiety and depression in adolescence and young adulthood.

4. Course and prognosis

There are no systematic long-term follow-up studies of children with AS as yet, partially because of nosologic issues. Many children are able to attend regular education classes with additional support services, although these children are especially vulnerable to being seen as eccentric and of being teased or victimized; others require special education services, usually not because of academic deficits but because of their social and behavioral difficulties. Asperger's initial description predicted a positive outcome for many of his patients, who were often able to utilize their special talents for the purpose of obtaining employment and leading self-supporting lives. His observation of similar traits in family members, i.e., fathers, may also have made him more optimistic about ultimate outcome. Although his account was tempered somewhat by the time he had seen 200 patients with the syndrome (25 years after his original paper), Asperger continued to believe that a more positive outcome was a central criterion differentiating individuals with his syndrome from those with Kanner's autism. Although some clinicians have informally concurred with this statement, particularly in regards to gainful employment, independence, and establishment of a family, no studies specifically addressing the long-term outcome of individuals with AS is currently available. The social impairment (particularly the eccentricities and social insensitivity), is thought to be lifelong.

Summary

Autism and Asperger syndrome are syndromes resulting from early-emerging and fundamental disruptions in the socialization process leading to a cascade of developmental impacts on social engagement and adaptation, communication and imagination, among other disabilities. Many areas of cognitive functioning are often preserved, and sometimes individuals with these conditions exhibit surprising if not prodigious skills. The early onset, symptom profile, and chronicity of these conditions implicate core biological mechanisms.²³ Advancements in genetics, neurobiology and neuroimaging (described elsewhere in this supplement), are concurrently

furthering our understanding of the nature of these conditions and of the formation of the social brain in typical individuals.²⁴ Together with the new wave of prospective studies of autism,²⁵ where siblings at risk for developing the condition are followed up from birth, a new social neuroscience perspective on the pathogenesis and pathobiology of factors is emerging. This effort is likely to elucidate the mysteries of the etiology and the pathogenesis of these conditions. Translational research into more efficacious treatment, if not prevention, will then hopefully follow.

References

1. Volkmar FR, Lord C, Bailey A, Schultz RT, Klin A. Autism and pervasive developmental disorders. *J Child Psychol Psychiatry*. 2004;45(1):135-70.
2. Rutter M. Genetic influences in autism. In: Volkmar F, Paul R, Klin A, Cohen D, editors. *Handbook of autism and pervasive developmental disorders*. 3rd ed. New York: Wiley; 2005. Volume 1, Section III, Chapter 16, p. 425-52.
3. Klin A, Pauls D, Schultz R, Volkmar F. Three diagnostic approaches to Asperger syndrome: implications for research. *J Autism Dev Disord*. 2005;35(2):221-34.
4. Fombonne E. Epidemiological studies of pervasive developmental disorders. In: Volkmar F, Paul R, Klin A, Cohen D, editors. *Handbook of autism and pervasive developmental disorders*. 3rd ed. New York: Wiley; 2005. Volume 1, Section I, Chapter 2, p. 42-69.
5. Kanner L. Autistic disturbances of affective contact. *Nerv Child*. 1943;2:217-50. (*Acta Paedopsychiatr*. 1968;35(4):100-36)
6. Rutter M. Diagnosis and definitions of childhood autism. *J Autism Dev Disord*. 1978;8(2):139-61.
7. Volkmar F, Klin A, Siegel B, Szatmari P, Lord C, Campbell M, Freeman BJ, Cicchetti DV, Rutter M, Kline W. Field trial for autistic disorder in DSM-IV. *Am J Psychiatry*. 1994;151(9):1361-7.
8. Editorial. A mercurial debate over autism. *Nat Neurosci*. 2005;8(9):1123.
9. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, Text Revised. Washington, DC: American Psychiatric Publishing Inc.; 2000.
10. National Research Council. *Educating children with autism*. Washington, DC: National Academies Press; 2001.
11. Werner E, Dawson G. Validation of the phenomenon of autistic regression using home videotapes. *Arch Gen Psychiatry*. 2005;62(8):889-95.
12. Klin A, Jones W, Schultz RT, Volkmar F. The enactive mind, from actions to cognition: lessons from autism. *Philos Trans R Soc Lond B Biol Sci*. 2003;358(1430):345-60.
13. Schultz RT. Developmental deficits in social perception in autism: the role of the amygdala and fusiform face area. *Int J Devl Neuroscience*. 2005;23(2-3):125-41.
14. Klin A, Saulnier C, Tsatsanis K, Volkmar F. Clinical evaluation in autism spectrum disorders: psychological assessment within a transdisciplinary framework. In: Volkmar F, Paul R, Klin A, Cohen D, editors. *Handbook of Autism and Pervasive Developmental Disorders*. 3rd ed. New York: Wiley; 2005. Volume 2, Section V, Chapter 29, p. 272-98.

15. Frith CD, Frith U. Interacting minds: a biological basis. *Science*. 1999;286(5445):1692-5.
16. Pennington BF, Ozonoff S. Executive functions and developmental psychopathology. *J Child Psychol Psychiatry*. 1996;37(1):51-87.
17. Hermelin B. Bright splinters of the mind: a personal story of research with autistic savants. London: Jessica Kingsley Publishers; 2001.
18. Howlin P. Outcomes in autism spectrum disorders. In: Volkmar F, Paul R, Klin A, Cohen D, editors. *Handbook of autism and pervasive developmental disorders*. 3rd ed. New York: Wiley; 2005. Volume 1, Section I, Chapter 7, p. 201-21.
19. Asperger H. 'Autistic Psychopathy' in childhood. (trans. U. Frith) In: Frith U. *Autism and Asperger Syndrome*. Cambridge: Cambridge University Press; 1944/1992. p. 37-62.
20. Wing L. Asperger's syndrome: a clinical account. *Psychol Med*. 1981;11(1):115-29.
21. Klin A, McPartland J, Volkmar FR. Asperger syndrome. In: Volkmar F, Paul R, Klin A, Cohen D, editors. *Handbook of autism and pervasive developmental disorders*. 3rd ed. New York: Wiley; 2005. Volume 1, Section I, Chapter 4, p. 88-125.
22. Fombonne E, Tidmarsh L. Epidemiologic data on Asperger disorder. *Child Adolesc Psychiatric Clin N Am*. 2003;12(1):15-21, v-vi.
23. Klin A, Jones W, Schultz R, Volkmar F, Cohen D. Defining and quantifying the social phenotype in autism. *Am J Psychiatry*. 2002;159(6):895-908.
24. Schultz RT, Romanci LM, Tsatsanis KD. Neurofunctional models of autistic disorder and Asperger syndrome: clues from neuroimaging. In: Klin A, Volkmar FR, Sparrow SS, editors. *Asperger Syndrome*. New York: Guilford Press; 2000. p. 172-209.
25. Zwaigenbaum L, Bryson S, Rogers T, Roberts W, Brian J, Szatmari P. Behavioral manifestations of autism in the first year of life. *Int J Dev Neurosci*. 2005;23(2-3):143-52.