Rev Bras Psiquiatr 2003;25(2):103-9

revisão

Asperger syndrome: an update

Síndrome de Asperger

Ami Klin

Child Psychology and Psychiatry Yale Child Study Center. New Haven, CT, USA

Abstract This article provides an overview of the history and clinical features of Asperger syndrome, and considers guidelines for clinical assessment and treatment. A review of issues related to external validity is provided, which points out the limitations of current research, and lists several potentially beneficial areas of investigation into the nosologic status of the condition. It concludes with a discussion of the unequivocal need of individuals with severe social disabilities for comprehensive and adequate educational services and other treatments irrespective of the fact that the validity and the utility of this specific diagnostic concept is far from resolved.

Keywords Asperger syndrome. Pervasive developmental disorder.

Resumo Esse artigo realiza uma revisão da história e do quadro clínico da síndrome de Asperger, considerando orientações para a avaliação clínica e o tratamento. Aspectos da validade dessa entidade nosográfica, as limitações das pesquisas atuais e as potenciais vantagens dessa linha de investigação são revisadas. Conclui discutindo a necessidade da implementação de serviços educacionais e o estabelecimento de outras intervenções de maneira adequada para o atendimento de indivíduos com graves alterações da sociabilidade, independentemente da validade e utilidade desse diagnóstico.

Descritores Síndrome de Asperger. Transtorno global do desenvolvimento.

Introduction

Asperger syndrome (AS) is one of the pervasive developmental disorders (PDD), which are a family of congenital conditions characterized by marked social impairment, communication difficulties, play and imagination deficits, and a range of repetitive behaviors or interests.[1] The prototypical PDD is autism, which was first described by Leo Kanner at Johns Hopkins in 1943.[2] Autism occurs in 1 out of every 1,000 births,[3] is a neurobiological disorder with a strong genetic component (a 2% to 5% recurrence rate in siblings, which is a 50 fold increase relative to the general population),[4] and some, as yet tentative biological markers involving brain structure (e.g., some individuals may have larger brains) and brain function (e.g., the typical brain specialization to recognize faces is not present).[5] About 70% of individuals with autism have a degree of mental retardation, and the typical cognitive profile includes great variability of skills (e.g., usually higher level nonverbal problem-solving skills and lower level language and conceptual skills).[6] Universally, there is a considerable discrepancy between a person's cognitive potential (i.e., their IQ s) and their ability to meet the demands of everyday life (or adaptive skills).[7] The diagnosis of autism is entirely behavioral, through clinical examination of a child's history and current presentation in the areas of social, communicative, and play/imagination behaviors.[8] In the past decade, there has been progress in research of the biological origins of autism, particularly in the areas of genetics and brain function, but there is no biological test as yet (e.g., through blood analysis) to identify individuals with this condition.

In 1944, Hans Asperger, an Austrian pediatrician with interest in special education, described four children who had difficulty integrating socially into groups.[10] Unaware of Kanner's description of early infantile 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

This work was partly supported by grants P01 HD 03008 and P01 HD/DC35482 from the National Institute of Child Health and Human Development, Bethesda, MD.
Recieved on 7/8/2002. Approved on 2/4/2002.

and a tendency to intellectualize emotions, an inclination to engage in long winded, one-sided, sometimes incoherent and rather formalistic speech (he called them "little professors"), all-absorbing interests involving unusual topics that 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 in fact could not be diagnosed in the first years of life. Discarding the possibility of a psychogenetic 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.[11] Her codification of the condition, which she called Asperger's syndrome (AS), 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 Asperger's syndrome 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.[12] Although AS was first granted official recognition in ICD-10,[13] and appears as Asperger's disorder in DSM-IV,[1] its nosological status is still uncertain.

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.[1]

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 other people, typically approaching 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 Asperger's syndrome develop symptoms of a 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.[12]

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.[14] 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 (assertions of fact, humorous remarks, etc.). 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.[12] 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 ubiqui-

tous. However, in both younger and older children typically the special interests interfere with learning in general because they absorb some much of the child's attention and motivation, and also interfere with the child's ability to engage in more reciprocal forms of conversation with others.

Individuals with AS may have a history of delayed acquisition of motor skills such as pedalling a bike, catching a ball, opening jars, and climbing outdoor play equipment. They are often visibly awkward and poorly coordinated and may exhibitid stilted or bouncy gait patterns and odd posture. Neuropsychologically, there may be 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.[15] Many children exhibit high levels of activity in early childhood, and the commonest reported comorbid symptoms in adolescence and young adulthood are anxiety, and particularly depression.[16]

Clinical assessment

AS, like the other pervasive developmental disorders, involves delays and deviant patterns of behavior in multiple areas of functioning. To thoroughly evaluate all relevant domains, different areas of expertise, including overall developmental functioning, neuropsychological features, and behavioral status are required. Hence the clinical assessment of individuals with this disorder is most effectively conducted by an experienced interdisciplinary team. In the majority of cases, a comprehensive interdisciplinary assessment will involve the following components: a thorough developmental and health history, psychological and communication assessments, and a diagnostic examination including differential diagnosis.[17] Further consultation regarding behavioral management, motor disabilities, possible neurological concerns, psychopharmacology, and assessment related to advanced studies or vocational training may also be needed. Given the prevailing difficulties in the definition of AS, and the great heterogeneity of the condition, it is crucial that the aim of the clinical assessment be a comprehensive and detailed profile of the individual's assets, deficits, and challenges, rather than simply a diagnostic label. Effective educational and treatment programs can only devised on the basis of such profile, given the need to address specific deficits while capitalizing on the person's various resources and strengths.

The psychological assessment aims at establishing the overall level of intellectual functioning, profiles of psychomotor functioning, verbal and nonverbal cognitive strengths and weaknesses, style of learning, and independent living skills. At a minimum, the psychological assessment should include assessments of intelligence and adaptive functioning, although the assessment of more detailed neuropsychological skills can be of great help to further delineate the child's profiles of strengths and deficits (e.g., organizational skills). A description of results should include not only quantified information but also a judgment as to how representative the child's performance was during the assessment procedure, and a description of the conditions that are likely to foster optimal and diminished performance. For example, the child's responses to the amount of structure imposed by the adult, the optimal pace for presentation of tasks, successful strategies to facilitate learning form modeling and demonstrations, effective ways of containing off-task and maladaptive behaviors such as cognitive and behavioral rigididty (e.g., perseverations, perfectionism, rituralized behavior), distractibility (e.g., difficulty inhibiting irrelevant responses, tangentiality), and anxiety, are all important observations that can be extremely useful for designing an appropriate intervention program. Within the psychological assessment, particular attention should be place on adaptive functioning, which refers to capacities for personal and social self-sufficiency in real-life situations. The importance of this component of the clinical assessment cannot be overemphasized. Its aim is to obtain a measure of the child's typical patterns of functioning in familiar and representative environments such as the home and the school, which may contrast markedly with the demonstrated level of performance and presentation in the clinic. It provides the clinician with an essential indicator of the extent to which the child is able to utilize his or her potential (as measured in the assessment) in the process of adaptation to environmental demands. A large discrepancy between intellectual level and adaptive level signifies that a priority should be made of instruction within the context of naturally occurring situations in order to foster and facilitate the use of skills to enhance quality of life.

The communication assessment should examine nonverbal forms of communication (e.g., gaze, gestures), nonliteral language (e.g., metaphor, irony, absurdities, and humor), suprasegmental aspects of speech (e.g., patterns of inflection, stress and volume modulation), pragmatics (e.g., turn-taking, sensitivity to cues provided by the interlocutor), and content, coherence, and contingency of conversation. Particular attention should be given to perseveration on circumscribed topics, metalinguistic skills (e.g., understanding of the language of mental states including intentions, emotions, and beliefs), reciprocity, and rules of conversation.

The diagnostic assessment should integrate information obtained in all components of the comprehensive evaluation, with a special emphasis on developmental history and current symptomatology. It should include observations of the child during more and less structured periods. This effort should take advantage of observations in all settings, including the clinic's reception area (e.g., contacts with other children or with family members), the halls (e.g., how the child interacts initially with the examiners), as well as in the testing room during breaks, periods of silence, or otherwise unstructured situations. Quite often, the child's disability is much more apparent during such periods in which the child is not given any instruction and has no adult-imposed expectation as to how to behave. Specific areas for observation and inquiry include the patient's patterns of special interest and leisure time, social and affective presentation, quality of attachment to family members, development of peer relationships and friendships, capacities for self-awareness, perspective-taking and level of insight into social and behavioral problems, typical reactions in novel situations, and

ability to intuit other person's feelings and infer other person's intentions and beliefs. Problem behaviors that are likely to interfere with remedial programming should be noted (e.g., anxiety, temper tantrums). The children's ability to understand ambiguous nonliteral communications (particularly teasing and sarcasm) should be further examined, particularly in regards to the child's patterns of response (e.g., misunderstandings of such communications may elicit aggressive behaviors). Other areas of observation involve the presence of obsessions or compulsions, ritualized behaviors, depression and panic attacks, integrity of thought, and reality testing.

Treatment

As in autism, treatment of AS is essentially supportive and symptomatic, and to a great extent, overlap with the treatment guidelines applicable to individuals with autism unaccompanied by mental retardation.[18] One initial difficulty encountered by families is proving eligibility for special services. As individuals with AS are often very verbal and many of them do well academically (at least in some areas), educational authorities might judge that the deficits – primarily social and communicative – are not within the scope of educational intervention. In fact, these two aspects should be the core of any educational interention and curriculum for individuals with this condition. In regards to learning strategies, skills, concepts, appropriate procedures, cognitive strategies, and behavioral norms may be more effectively taught in an explicit and rote fashion using a parts-to-whole verbal instruction approach, where the verbal steps are in the correct sequence for the behavior to be effective. Additional guidelines should be derived from the individual's neuropsychological profile of assets and deficits. The acquisition of self-sufficiency skills in all areas of functioning should be a priority. The tendency of individuals with AS to rely on rigid rules and routines can be used to foster positive habits and enhance the person's quality of life and that of family members. Specific problem-solving strategies, usually following a verbal algorithm, may be taught for handling the requirements of frequently occurring, troublesome situations (e.g., involving novelty, intense social demands, or frustration). Training is usually necessary for recognizing situations as troublesome and for selecting the best available learned strategy to use in such situations. Social and communication are best taught by a communication specialist with an interest in pragmatics in speech in the context of both individual and small group therapy. Communication therapy should include appropriate nonverbal behaviors (e.g., the use of gaze for social interaction, monitoring and patterning of inflection of voice), verbal decoding of nonverbal behaviors of others, social awareness, perspective-taking skills, and correct interpretation of ambiguous communications (e.g., nonliteral language). Often, adults with AS fail to meet entry requirements for jobs in their area of training (e.g., college degree) or fail to maintain a job because of their poor interview skills, social disabilities, eccentricities, or anxiety attacks. It is important, therefore, that they are trained for and placed in jobs for which they are not neuropsychologically impaired, and in which they will enjoy a certain degree of support and shelter. It is also preferable that the job does not involve intensive social demands, time pressure, or the need to quickly improvise or generate solutions to novel situations. The little experience available with self-support groups suggests that individuals with AS syndrome enjoy the opportunity to meet others with similar problems and may develop relationships around an activity or subject of shared interest. Special interests may be utilized as a way of creating social opportunities through hobby groups. Supportive psychotherapy as well as pharmacological interventions may be helpful in dealing with feelings of despondency, frustration, and anxiety, although a more direct, problem-solving focus is taught to be more beneficial than an insight-oriented approach.

External validity

Although AS was first described over 50 years ago,[10] it was not until 1994 that is was included in DSM-IV[1] as one of the PDDs. Inclusion in the DSM-IV followed limited evidence that it could be differentiated from autism unaccompanied by mental retardation, or higher functioning autism (HFA).[19] As noted, however, its nosological status remains unclear, in part due to the adoption of varying diagnostic schemes in the research literature.[12] Although the advent of the DSM-IV definition was intended to create a consensual diagnostic starting point for research, it has been consistently criticized as overly narrow,[20,21] rendering the diagnostic assignment of AS improbable or even "virtually impossible".[22,23]

The introduction of AS in DSM-IV and ICD-10[13] was prompted by the recognition that autism is a clinically heterogeneous disorder and that the characterization of subtypes of PDD might help behavioral and biological research by allowing the identification of clinically more homogeneous groups.[24-26] While this effort has been successful for some PDD conditions (e.g., Rett syndrome),[27] it has not been the case in AS. Published reports have modified DSM-IV or ICD-10 criteria,[15,28] treated AS and HFA interchangeably, [16,17, 29,30] or used unique investigator-defined criteria,[31] making it difficult to compare studies. Only two studies[32,33] have systematically compared different diagnostic schemes. These two studies generally revealed that different nosologic schemes result in the assignment of different diagnoses to the same patients, raising the important issue of how to compare studies utilizing different definitions of AS. However, these studies did not consider the question of the utility of a given diagnostic concept relative to important predictions that may have practical value to research (e.g., differences in neuropsychological or neurobiological findings between AS and HFA), or clinical practice (e.g., differences in treatment efficacy, comorbid symptomatology, or outcome as a function of the given diagnostic assignment).[34] To summarize, the state of discussions on the nosologic status of AS is, therefore, extremely problematic, given that studies cannot be necessarily compared because of the adoption of different diagnostic definitions, and there has been no comparison across different diagnostic schemes in regards to the relative utility of each of the schemes. And yet, the absence of a con-

sensual or validated definition has not deterred the upsurge of research publications on the syndrome nor the apparently marked increased in the use of the diagnosis in clinical and educational settings.[35]

It is apparent from this brief discussion of the external validity of AS that studies comparing the utility of different diagnostic schemes is badly needed. This agenda for research is needed for several reasons: First, there is a need to gauge the extent to which available research data obtained using different diagnostic systems are comparable. Second, despite the upsurge in research and clinical interest in AS, the absence of a validated definition prevents the development of standardized instrumentation that could enhance reliability of diagnostic assignment and make possible cross-site collaborations that are essential to both behavioral and biological research. Third, there are indications that the DSM-IV definition is being ignored in clinical practice,[23] with the term being used as synonymous to HFA or, maybe even more commonly, to PDD-NOS,[12] creating a rift between DSM-IV and research and clinical practice, thus confusing and alienating investigators, clinicians, and parents alike. And fourth, the scientifically interesting question as to whether or not there are qualitative discontinuities among the PDDs, or alternatively, whether the PDDs should be considered along a dimensional continuum (and what this dimension should be) is left unresolved without some resolution of the validity of the AS diagnosis.

Several lines of research could serve the purpose of assessing the utility of different diagnostic schemes. First, learning profiles of assets and deficits are of great importance in educational treatment planning for individuals with PDDs,[6] particularly in individuals with normative IQs.[17] Neuropsychological research of AS is extremely equivocal to date. In 1995, our group[15] documented considerable differences between individuals with HFA and AS. Specifically, individuals with AS showed a profile of assets and deficits consistent with a nonverbal learning disability (NLD).[36] NLD is characterized by strengths in verbally-mediated skills (e.g., vocabulary, rote knowledge, verbal memory, verbal output) and deficits in nonverbal skills (e.g., visual-spatial problem solving, visual-motor coordination). Individuals with HFA exhibited the opposite profile. Such "double dissociation" has been shown to be one of the most powerful external validators of specific subtypes of syndromes.[37] These findings have been supported by a number of studies focused on IQ profiles,[38-40] although several other studies have failed to replicate them.[21,41] However, as noted, direct comparison across studies is not possible since different diagnostic schemes were used in them.

A second potential area of validation research in AS could utilize patterns of comorbidity. Research on the psychiatric difficulties associated with the PDDs is of great importance for treatment planning given that these symptoms may have the potential of being extremely debilitating, e.g., limiting the effectiveness of educational interventions, posing further limitations on the individual's ability to utilize his or her internal coping resources. Documentation of these difficulties can lead to psychopharmacological approaches that can greatly alleviate such symptoms, thus making the student more available to other forms of intervention, e.g., educational. AS has been associated with a host of comorbid conditions, including schizophrenia,[42,43] Tourette's syndrome,[44] attentional, affective, and obsessional disorders.[45,46] More recent research has emphasized anxiety, mood and obsessional disorders to be particularly prevalent in this population.[47,48] As previously, however, there has been no attempt to study patterns of comorbidity that may be specific to HFA and AS, with most studies using the two diagnoses interchangeably.

A third potential line of research for external validation studies of AS relates to the aggregation of social and other psychiatric disorders in family relatives. Research into patterns of genetic liability associated with the PDDs has been one of the most active areas of investigation in autism and related conditions.[4] Studies have consistently shown higher rates of social disabilities or difficulties in family members of individuals with autism,[49,50] as well as of other psychiatric symptoms including anxiety, mood, and obsessional disorders.[51,53] None of these studies, however, has made the attempt to assess the utility of separating families of probands with HFA from those of probands with AS. The available data on the familiality of AS are essentially limited to a handful of case reports and some preliminary studies.[53,54] Many case reports have been consistent with Asperger's original observation[10] of similar traits in family members, particularly fathers or male relatives.[55-57] Whether or not variants of autism such as AS might reflect greater or lower genetic liability could be of great significance in elucidating mechanisms involved in producing the marked heterogeneity among PDDs. Such studies, however, cannot be conducted without standardized diagnostic procedures, which, in turn, depend upon some initial consensus as to criteria for the definition of AS.

In order to avoid insularity among research groups (i.e., each one adopting its own diagnostic scheme) and to advance the field from its current stalemate, on approach might be to simultaneously compare different diagnostic schemes and assess each one on the basis of independent factors of clinical or research significance. Such research is not yet available.

Future directions for research and clinical service

The current state of affairs in nosologic research of AS, with little available evidence to point to a distinction between this concept and HFA and PDD-NOS, as well as other similar diagnostic entities,[12] has prompted many investigators to derive premature conclusions. For example, some have treated AS as different than other conditions, whereas others have treated as the same as other conditions. The more typical approach is to see AS within the spectrum of PDDs, maybe indicating some half point between autism and normalcy. Our discussion suggests that either position is unwarranted at present. Those who view AS as different from other disorders have the onus to document in what ways is AS unique among the social disabilities. This task requires comparison of extant diagnostic schemes. Those who view AS a within the spectrum of social disabilities have the onus to define what this spectrum consists

of. This task requires isolation of specific psychological (e.g., IQ, language functions, metacognitive skills) or neurobiological (e.g., genetic liabilities, neurostructure or neurofunction findings) that can quantify the social disability spectrum and predict social outcome. Both of these programmatic research areas are still in their incipience.

It is nevertheless crucial to separate this research discussion from the areas of clinical practice and provision of services dedicated to individuals with AS and their families. The unavoidable confusion conveyed to parents and advocates inherent in the fragility of the validity status of AS is sufficiently harmful to justify a concerted effort on the part of clinicians and advocates to adhere to some unequivocal principles so that the needs of their clients are properly addressed. First, whether or not there is controversy over the fine-grained distinctions between AS and other conditions, and despite some literature and great media coverage over some famous individuals exhibiting or not this condition, the vast majority of children, adolescents, and adults with AS require a comprehensive package of treatments. Equivocating about these individuals' needs on the basis of the poor scientific status of the diagnostic concept is unjustified. Second, adequate educational programs should not be based on a diagnostic label and generalizations associated with it, but on individualized profiles of assets and deficits, which can only be accomplished through thorough evaluations involving psychological, communication, and psychiatric assessments. And third, the notion that AS is simply a 'milder' form of autism, regardless of whether or not this statement is scientifically justified, should be well-contextualized in that whereas 'mild' is a term comparing individuals with this condition with those with prototypical autism and a degree of mental retardation, and it is certainly not 'mild' when comparing these individuals great difficulties in meeting the demands of everyday life. In other words, eligibility for services should be fiercely advocated. Treatment should focus on those areas of greatest challenges, and which are known to deleteriously impact on these individuals capacity for independent living, vocational satisfaction, and better social adjustment. These include socialization skills in general (e.g., social reciprocity and social communication), adaptive skills (e.g., "street smarts", how to function in the community, how to fend for oneself in potentially inhospitable environments), organizational skills (e.g., how to perform complex tasks and anticipate problems), a cognitive-behavioral, and sometimes psychopharmacological plan to alleviate anxiety and depression when these emerge, and sympathetic mental health and educational professionals who strive to building upon these individuals' unique assets to compensate for their deficits and to create more positive social experiences.

References

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. Text Revision. DSM-IV-TR. Washington (DC): American Psychiatric Association; 2000.
2. Kanner L. Autistic disturbances of affective contact. Nervous Child 1943;2:217-53.
3. Fombonne E. The epidemiology of autism: a review. Psychol Med 1999;29:769-86.
4. Rutter M. Genetic studies of autism: from the 1970s into the millennium. J Child Psychol Psychiatry 2000;28:3-14.
5. Schultz RT, Romanski LM, Tsatsanis KD. Neurofunctional models of autistic disorder and Asperger syndrome: clues from neuroimaging. In: Klin A, Volkmar F, Sparrow S, eds. Asperger Syndrome. New York: Guilford Press; 2000. p. 172-209.
6. Klin A, Carter A, Volkmar FR, Cohen DJ, Marans WD, Sparrow SS. Assessment issues in children with autism. In: Cohen DJ, Volkmar FR, eds. Handbook of Autism and Pervasive Developmental Disorders. 2nd ed. New York: Wiley; 1997. p. 411-8.
7. Gillham JE, Carter AS, Volkmar FR, Sparrow SS. Toward a developmental operational definition of autism. J Autism Dev Disord 2000;30(4):269-78.
8. Lord C. Diagnostic instruments in autism spectrum disorders. In: Cohen DJ, Volkmar FR, eds. Handbook of Autism and Pervasive Developmental Disorders. 2nd ed. New York: Wiley; 1997. p. 460-83.
9. Bailey A, Phillips W, Rutter M. Autism: towards an integration of clinical, genetic, neuropsychological, and neurobiological perspectives. J Child Psychol Psychiatry 1996;37(1):89-126.
10. Asperger H. Die 'Autistischen Psychopathen' im Kindesalter. Archiv für Psychiatrie und Nervenkrankheiten 1944;117:76-136.
11. Wing L. Asperger's syndrome: a clinical account. Psychol Med 1981;11:115-29.
12. Volkmar FR, Klin A. Diagnostic issues in Asperger syndrome. In: Klin A, Volkmar FR, Sparrow SS, eds. Asperger syndrome. New York: Guilford Press; 2000. p. 25-71.
13. World Health Organization. The ICD-10 classification of mental and behavioral disorders. Geneva: World Health Organization; 1992.
14. Klin A, Volkmar FR. Asperger Syndrome. In: Cohen DJ, Volkmar FR, eds. Handbook of Autism and Pervasive Developmental Disorders. New York: Wiley & Sons; 1997. p. 94-122.
15. Klin A, Volkmar FR, Sparrow SS, Cicchetti DV, Rourke BP. Validity and neuropsychological characterization of Asperger syndrome. J Child Psychol Psychiatry 1995;36:1127-40.
16. Martin A, Patzer DK, Volkmar FR. Psychopharmacological treatment of higher-functioning pervasive developmental disorders. In: Klin A, Volkmar FR, Sparrow SS, eds. Asperger syndrome. New York: Guilford Press; 2000. p. 210-30.
17. Klin A, Sparrow SS, Marans WD, Carter A, Volkmar FR. Assessment issues in children and adolescents with Asperger syndrome. In: Klin A, Volkmar FR, Sparrow SS, eds. Asperger syndrome. New York: Guilford Press; 2000. p. 309-39.
18. Klin A, Volkmar FR. Treatment and intervention guidelines for individuals with Asperger syndrome. In: Klin A, Volkmar FR, Sparrow SS, eds. Asperger syndrome. New York: Guilford Press; 2000. p. 340-66.
19. Volkmar FR, Klin A, Siegel B, Szatmari P, Lord C, Campbell M, et al. DSM-IV Autism/Pervasive Developmental Disorder Field Trial. Am J Psychiatry 1994;151:1361-7.
20. Eisenmajer R, Prior M, Leekam S, Wing L, Gould J, Welham M, Ong B. Comparison of clinical symptoms in autism and Asperger's disorder. J Am Acad Child Adolesc Psychiatry 1996;35:1523-31.
21. Szatmari P, Archer L, Fisman S, Streiner DL, Wilson F. Asperger's syndrome and autism: differences in behavior, cognition, and adaptive functioning. J Am Acad Child Adolesc Psychiatry 1995;34:1662-71.
22. Miller J, Ozonoff S. The external validity of Asperger disorder: lack of evidence from the domain of neuropsychology. J Abnorm Psychol 2000;109:227-38.

23. Mayes SD, Calhoun SL, Crites DL. Does DSM-IV Asperger's Disorder exist? J Abnorm Child Psychol 2001;29:263-71.
24. Rutter M. The Emanuel Miller Memorial Lecture 1998. Autism: two-way interplay between research and clinical work. J Child Psychol Psychiatry 1999;40:169-88.
25. Bailey A, Palferman S, Heavey L, Le Couteur A. Autism: the phenotype in relatives. J Autism Dev Disord 1998;28:369-92.
26. Volkmar FR, Klin A, Cohen DJ. Diagnosis and classification of autism and related conditions: consensus and Issues. In: Cohen DJ, Volkmar FR, eds. Handbook of autism and pervasive developmental disorders. New York: Wiley; 1997. p. 5-40.
27. Gura T. Gene defect linked to Rett syndrome. Science 1999;286(5437):27.
28. Ozonoff S, Rogers S, Pennington B. Asperger's syndrome: evidence of an empirical distinction. J Child Psychol Psychiatry 1991;32:1107-22.
29. Gillberg C, Gillberg C, Rastam M, Wentz E. The Asperger syndrome (and high-functioning autism) Diagnostic Interview (ASDI): a preliminary study of a new structured clinical interview. Autism 2001;5:57-66.
30. Howlin P. Outcome in adult life for more able individuals with autism or Asperger syndrome. Autism 2000;4:63-83.
31. Gillberg C. Asperger syndrome and high-functioning autism. Brit J Psychiatry 1998;172:200-9.
32. Ghaziuddin M, Tsai LY, Ghaziuddin N. Brief report: a comparison of the diagnostic criteria for Asperger syndrome. J Autism Dev Disord 1992;22(4):643-9.
33. Leekam S, Libby S, Wing L, Gould J, Gillberg C. Comparison of ICD-10 and Gillberg's criteria for Asperger syndrome. Autism 2000;4:11-28.
34. Szatmary P. Perspectives on the classification of Asperger syndrome. In: Klin A, Volkmar FR, Sparrow SS, eds. Asperger syndrome. New York: Guilford Press; 2000. p. 403-17.
35. Klin A, Volkmar FR, Sparrow SS, eds. Asperger syndrome. New York: Guilford Press; 2000.
36. Rourke B. Nonverbal learning disabilities: the syndrome and the model. New York: Guilford Press; 1989.
37. Fletcher JM. External validation of learning disability typologies. In: Rourke PB, ed. Neuropsychology of learning disabilities: essentials of subtype analysis. New York: Guilford Press; 1985. p. 187-211.
38. Ehlers S, Nyden A, Gillberg C, Dahlgren Sandberg A. Asperger syndrome, autism and attention disorders: a comparative study of the cognitive profiles of 120 children. J Child Psychol Psychiatry 1997;38(2):207-17.
39. Lincoln A, Courchesne E, Allen M, Hanson E, Ene M. Neurobiology of Asperger syndrome: seven case studies and quantitative magnetic resonance imaging findings. In: Schopler E, Mesibov G, Kunce LJ, eds. Asperger syndrome or high-functioning autism? New York: Plenum; 1998. p. 145-66.
40. Lincoln AJ, Allen M, Kilman A. The assessment and interpretation of intellectual abilities in people with autism. In: Schopler E, Mesibov G, eds. Learning and cognition in autism. New York: Plenum; 1995. p. 89-117.
41. Ozonoff S. Neuropsychological function and the external validity of Asperger syndrome. In: Klin A, Volkmar FR, Sparrow SS, eds. Asperger syndrome. New York: Guilford Press; 2000. p. 72-96.
42. Clarke DJ, LittleJohns CS, Corbett JA, Joseph S. Pervasive developmental disorders and psychoses in adult life. British J Psychiatry 1989;155:692-9.
43. Tantam D. Annotation: Asperger's syndrome. J Child Psychol Psychiatry 1988;29:245-55.
44. Kerbeshian J, Burd L. Asperger's syndrome and Tourette syndrome: the case of the pinball wizard. Brit J Psychiatry 1986;148:731-6.
45. Ghaziuddin M, Tsai L, Ghaziuddin N. Comorbidity of autistic disorder in children and adolescents. Eur Child Adolesc Psychiatry 1992;1(4):209-13.
46. Thomsen PH. Obsessive-compulsive disorder in children and adolescents: a 6-22-year follow-up study: clinical descriptions of the course and continuity of obsessive-compulsive symptomatology. Eur Child Adolesc Psychiatry 1994;3:82-96.
47. Kim J, Szatmari P, Bryson S, Streiner DL, Wilson FJ. The prevalence of anxiety and mood problems among children with autism and Asperger syndrome. Autism 2000;4:117-32.
48. Green J, Gilchrist A, Burton D, Cox A. Social and psychiatric functioning in adolescents with Asperger syndrome compared with conduct disorder. J Autism Dev Disord 2000;30:279-93.
49. Piven J, Palmer P, Jacobi D, Childress D, Arndt S. The broader autism phenotype: evidence from a family study of multiple-incidence autism families. Am J Psychiatry 1997;154:185-90.
50. Murphy M, Bolton PF, Pickles A, Fombonne E, Piven J, Rutter M. Personality traits of the relatives of autistic probands. Psychol Med 2000;30:1411-24.
51. Piven J, Palmer P. Psychiatric disorder and the broad autism phenotype: evidence from a family study of multiple-incidence autism families. Am J Psychiatry 1999;156:557-63.
52. Bolton PF, Pickles A, Murphy M, Rutter M. Autism, affective and other psychiatric disorders: patterns of familial aggregation. Psychol Med 1998;28(2):385-95.
53. Folstein SE, Santangelo SL. Does Asperger syndrome aggregate in families? In: Klin A, Volkmar FR, Sparrow SS, eds. Asperger syndrome. New York: Guilford Press; 2000. p. 159-71.
54. Volkmar FR, Klin A, Pauls D. Nosological and genetic aspects of Asperger syndrome. J Autism Dev Disord 1998;28:457-63.
55. Bowman EP. Asperger's syndrome and autism: the case for a connection. British J Psychiatry 1988;152:377-82.
56. DeLong GR, Dwyer JT. Correlation of family history with specific autistic subgroups: Asperger's syndrome and bipolar affective disease. J Autism Dev Disord 1988;18(4):593-600.
57. Gillberg C, Gillberg IC, Steffenburg S. Siblings and parents of children with autism: a controlled population-based study. Dev Med Child Neurol 1992;34:389-98.

Correspondence:
Ami Klin
Child Psychology and Psychiatry
Yale Child Study Center
230 South Frontage Road
New Haven CT 06520
Tel.: (203) 785-3565
Fax: (203) 737-4197
E-mail: ami.klin@yale.edu