Autistic Behavior: Etiology and Evaluation

First described by Kanner (1943), autism is a behavioral syndrome, present from early life and defined by deficient social interaction, language and communication difficulties, and bizarre restricted or repetitive behavior patterns. At one time thought by some to be psychodynamically determined, it is now clear that the majority of autistic behaviors represent an observable manifestation of physiological dysfunction of one or more as yet undetermined brain systems (Lainhart, & Piven, 1995). In addition to characteristic features, many autistic persons display a variety of signs such as attention deficits, mental retardation, and seizures that are not specific to autism and hint at the high rate of comorbidity among the pervasive developmental disorders and other psychological/medical conditions. Variations in symptomology and in prognosis among autistic persons depend on both the severity and the extent of the underlying brain dysfunction, as well as the level of adaptive functioning.

Nosology

The diagnostic criteria for diagnosing autism are entirely behavioral. The most widely used criteria are those listed in the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) of the American Psychiatric Association (APA, 1994). Other analogous criteria are those of the International Classification of Diseases (10th revision) of the World Health Organization (ICD-10); those of investigators Rutter and Schopler (1987); and that of the National Society for Children and Adults with Autism (NSAC, 1978).

The DSM-IV classifies autistic disorder among the pervasive developmental disorders (PDD). PDD is a term introduced to set apart autism and similar disorders from mental retardation, developmental language disorders, and other specific learning disabilities on the one hand, and schizophrenia and schizoid-type personality disorders on the other.

To fulfill the criteria for autistic disorder according to the DSM-IV, persons must have been symptomatic since infancy or childhood and manifest a specified number of deficits that are out of keeping with their developmental level in each of three aspects of behavior. These include (1) qualitative impairment in reciprocal interaction, (2) qualitative impairment in verbal and nonverbal communication, and (3) a markedly restricted repertoire of activities and interests (APA, 1994).

To accommodate the entire spectrum of persons with autistic behaviors, DSM-IV classified persons with deficits in the these areas who meet fewer than the prescribed number of criteria for autistic disorder under the rubric “pervasive developmental disorder not otherwise specified.” Children with developmental learning disabilities due to lesions of the right hemisphere may be classified under pervasive developmental disorder not otherwise specified (Weintraub, & Mesulam, 1983), and the term
“disintegrative psychosis” has been used by some for children whose autistic symptomology follows an acute encephalopathy, for example an encephalitis, Reye’s syndrome, or a severe brain injury (Evans-Jones, & Rosenbaum, 1978).

Many parents and professionals consider the label “autistic” highly stigmatizing and avoid using it. To do so, some professionals may use such nonspecific terms as “emotionally disturbed” or erroneously use the term PDD for high-functioning autistic children, who in fact, fulfill the criteria for autism. For the same reason, they may use the term Asperger syndrome for highly verbal autistic children (Szatmari, Archer, Fisman, Streiner, & Wilson, 1995).

There is incomplete agreement regarding the nosological boundaries of autism. Some argue that if the definition of autism is behavioral, all persons who fulfill the behavioral criteria for autism should be considered autistic, whatever the etiology, associated symptomology, severity, and course of their encephalopathy (J. Matson, personal communication, October 2, 1997; Rutter, 1996). Others would reserve the term for individuals with an unknown etiology and a static course without blindness, deafness, or overt signs of brain dysfunction, like hydrocephalus or cerebral palsy. They would also exclude children with a known etiology like tuberous sclerosis or fragile X (Rutter, et al., 1987). While such a restricted definition may be useful for certain kinds of research, it goes beyond the purely behavioral criteria that define the syndrome. Those who take this view fully expect that, as biological markers for various conditions causing autistic symptomology are defined, autism will gradually be partitioned into a number of subtypes due to specific etiologies or to the dysfunction of specific brain systems. Possibly at some time in the future, these etiologically based diagnostic distinctions may prove useful for treatment planning, but current research progress has bolstered few argument in this favor.

Etiology

To understand the etiology of autism, it is convenient to divide the syndrome into nongenetic and genetic causes. Clinically, there is no distinction between these classifications; from all outward appearances, they are indistinguishable. The nongenetic causes are all associated with disruption, usually prenatal, to the normal pattern of brain development. Given this and the overlapping clinical picture, it seems reasonable to conclude that genetic forms of autism arise from mutations in genes controlling brain development and that both genetic and nongenetic etiologies cause damage to the same brain centers and regions [see later discussion] (Bachevalier, 1994; Gillberg, & Colman, 1996).

The principal nongenetic cause of autism is prenatal viral infection (Piven, Simon, Chase, Wzorek, Landa, Gayle, & Folstein, 1993). Chess (1977) reported that 8-13% of children born during the 1964 rubella pandemic developed autism along with the other birth defects associated with congenital rubella syndrome. Although other infectious agents
have also been associated with autism, these are mostly single cases. Taken together, they constitute additional evidence that prenatal infection can disrupt brain development in such a way that autism ensues. Prenatal toxoplasmosis, syphilis, varicella, and rubeola have been linked to single cases of autism. There are six reported cases of prenatal cytomegalovirus infection and autism, and eight cases of postnatal infection with mumps virus leading to autism, as well as a single case of herpes simplex infection (Markowitz, 1983; Piven, et al., 1993).

Although a popular notion exists that autism is associated with prenatal, perinatal, or neonatal trauma, there is in fact relatively little evidence to support the view (Piven, et al., 1993; Weir, & Salisbury, 1980). Nelson (1991) has examined the literature on autism and a variety of birth complications and reports no consistent or specific link between maternal history, pregnancy, delivery, or neonatal events and autism. Piven, et al. (1993) found slight support for the role of pre- and perinatal factors in the development of autism, but these factors seemed to play a larger role in cases of autism associated with severe mental retardation than in cases of high-functioning autism. Other nongenetic factors leading to autism may include hypothyroidism and maternal cocaine or alcohol use during pregnancy (Gillberg, et al., 1996).

There is considerable evidence that genetic factors play a role in the pathogenesis of autism. Three types of genetic associations have been described in the literature: (1) the familial aggregation of autism, per se—autism is more common in the sibs of affected children; (2) the familial aggregation of other disorders in the family members of autistic children—a variety of disorders that are mild, but probably conceptually related, have described in relatives; and (3) autism appears in association with a few particular disorders of known genetic etiology.

In most population-based studies, the prevalence of autism in the siblings of autistic children has been estimated to be about 2% to 3% (Rutter, 1968). And, while this number appears small, according to data presented by Lotter (1966) it is 50 to 100 times greater than the expected rate of autism of 4 to 5 per 10,000 in the population. It may also be an underestimate of the actual risk to siblings. Because autism is a severe disorder that has a devastating impact on family life, many families with an autistic child choose to limit further childbearing (Jones, & Szatmari, 1988). The decision not to have further children after the birth of the proband decreases the prevalence of autism in siblings. Taking “stoppage rules” into account by measuring the recurrence risk of autism in siblings raises the estimate of the risk of autism to siblings to rates higher than the previously reported 2% to 3% (Jones, et al., 1988). Using this approach, in a statewide family study of autism, Ritvo, Jorde, & Mason-Brothers (1989) reported a risk of autism for siblings born after the proband (recurrence risk) of 8.6%; if the first autistic child was male, the recurrence risk was 7%, and if the first autistic child was female, the recurrence risk was 14.5%.
Twin studies also suggest a genetic basis for autism. Folstein & Rutter (1977) studied pairs of same-sex twins, with diagnosis of the second twin made blind to the affected status of the first. They found concordance in four of eleven (36%) monozygotic (MZ) twins and in zero of ten (0%) dizygotic (DZ) twins. Steffenberg & Gillberg (1986) found even greater differences between monozygotic (91%) and dizygotic (0%) twins in a population-based study in Northern Europe. These studies all reveal a much greater degree of concordance in monozygotic than dizygotic twins and, therefore, suggest a substantial genetic component in autism. Adoptive twin studies would allow an even clearer differentiation of genetic and environmental factors. To date, however, adoptive twin studies have not been reported in the literature, probably because it has not been possible to identify a large sample of twin pairs, with at least one autistic proband, that have been reared apart.

The study of family members was prompted by the clinical observations of social oddities in some parents and by the frequent report in both parents and siblings of a history of developmental disorders of reading and spelling. These deficits have more recently been documented using standardized assessments. The twin study of Folstein, et al. (1977) found a higher rate of cognitive deficits (i.e., reading, spelling, and articulation disorders; language delay and mental retardation) in the nonautistic MZ co-twins (6/7) than in the nonautistic DZ co-twins (1/10). The concordance rate for cognitive difficulties, including those diagnosed as autistic, was 82% for MZ pairs and 10% for DZ pairs. These findings suggest that cognitive abnormalities may be a milder but conceptually related expression of an underlying genetic abnormality in autism, and that familial transmission of autism involves a mild form of the disorder. Such a view accounts for some cases in which autistic probands do not have a close family member who fits the diagnostic criteria for autism; if an expanded autistic phenotype can be shown to include a mild form of autism, then the sibling frequencies may be found to approach those predicted by simple genetic models (Folstein, & Rutter, 1988). A high-functioning form of autism also may explain how the gene or genes for the disorder can be maintained in the gene pool although autistic individuals rarely reproduce.

Several studies have reported the aggregation of particular psychological disorders in the family members of autistic individuals (reviewed in Piven, Chase, & Landa, 1992). Early studies of autism suggested that schizophrenia aggregated in the families of autistic children. These early studies could not be replicated and were most likely the result of the overly inclusive diagnostic criteria used to define both autism and schizophrenia (Rutter, et al., 1987). Two studies (one using family history method and the other using DSM-III criteria for autism) have reported rates of major affective disorder in the family members of autistic individuals that were significantly higher than those from published epidemiologic studies (Cantwell, Baker, & Rutter, 1978; Piven, Gayle, & Chase, 1989). However, neither study incorporated a control group for direct comparison. When parents were assessed using a structured clinical interview, they were found to have significantly higher rates of anxiety disorders compared with control subjects (Piven, et al., 1989). Recurrent major affective disorder was also more common in the parents of
autistic probands, although the difference compared with control subjects did not reach statistical significance. Neither anxiety disorders nor affective disorders could be explained as a result of the stress of having an autistic child as the onset of these disorders had, in most cases, occurred prior to the birth of the proband.

Most of the studies discussed above which have demonstrated the familial aggregation of autism and other disorders in family members have excluded cases of autism in which the proband has a concurrent medical condition of known genetic etiology. Of interest in the quest for the etiologic definition are the occasional cases that are seen in association with particular genetic conditions.

Fragile X (FraX) is a cytogenetic marker located at Xq27.3 which is associated with the fragile X syndrome (Gillberg, et al., 1996). This X-linked mental retardation syndrome is the second most common known genetic cause of mental retardation, and the FraX marker has also been reported to be significantly associated with the syndrome of autism (Gillberg, et al., 1996). Ritvo, et al. (1989) reported a pooled prevalence estimate based upon the screening of 614 autistic males reported in 12 studies of 7.7%. Brown, Jenkins, & Cohen (1986) suggest that autism may occur with fragile X because of the involvement of a gene for affective disorder separate from and loosely linked with the FraX marker.

Associations have also been described between autism and several other genetic disorders including tuberous sclerosis, untreated phenylketonuria, and possibly neurofibromatosis (Gillberg, et al., 1996). For the most part, these few reports have not been based on standardized assessments of autism and samples have not been systematically collected. Taken together, the proportion of cases of autism that are accounted for by the aggregate of these specific genetic etiologies is small. The great majority of cases are of unknown etiology, but, as discussed earlier, there is considerable evidence that genetic factors are important.

Further possible clues to the etiological factors inherent to autism are to be found in the aberrant brain system neuropathology commonly reported to occur in autistic individuals. Many regions of the cerebrum have been posited as loci of autism. In fact, autism affects so many abilities and behaviors that it is difficult to find in the literature a brain region, which has not been put forth as a possible site of dysfunction. Proposed sites have included the limbic system, brainstem, basal ganglia, vestibular system, and cerebellum. Damasio & Maurer (1978), focusing on autistic deficits in executive function, highlighted the medial frontal lobes and the basal ganglia as sites of dysfunction. In their discussion of the medial frontal lobes, they placed particular emphasis on the role of the cingulate gyrus; a part of the limbic system closely tied to memory processes. Their hypothesis was based on similarities between the behavior observed in individuals with autism and in adults with acquired medial frontal or basal ganglia lesions. A hypothesis put forth by Ornitz (1983) suggested those autistic difficulties with sensory modulation and with sensorimotor response could best be explained by a malfunction of brainstem and diencephalic networks that gate sensory
input. Deficits in higher-order capacities such as language, Ornitz proposed, are consequences of the abnormal input supplied to the cerebrum by these malfunctioning gating systems. Another possible explanation for the stimulus overselectivity manifested in autism is a developmental spatial neglect syndrome (Bryson, Wainwright-Sharp, & Smith, 1990), akin to the acute spatial neglect that follows parietal lobe injury. These authors reviewed a number of autonomic, electrophysiological and behavioral studies indicating the existence of attentional anomalies in individuals with autism and they describe similarities between the behavior of individuals with autism and that of patients with left-sided neglect. Hetzler and Griffin (1981) and DeLong (1992), recognizing the similarities between autistic behavior and Klüver-Bucy Syndrome, have characterized autism as the effect of developmental dysfunction in structures of the medial temporal lobe, especially the hippocampus and amygdala. This theory incorporates an observation that the effect of a lesion in a developing brain often is more severe than or is distinct from the effect of a similar lesion in a mature brain, because brain systems downstream from the lesion may depend on correct input for their proper maturation. This is supported by Bachevalier's (1994) finding that lesions of medial temporal lobe structures induced in neonatal monkeys result in behaviors which are more typical of autism than similar lesions induced in adult monkeys.

As well as the aforementioned anatomical systems, quite a few chemical systems have been thought to underlie autism. The finding of hyperserotonemia in some individuals with autism has been widely replicated (Cook, 1990). Levels of the other monoamines also have been found to be higher than normals in individuals with autism (Martineau & al. 1992). Panksepp (1979), on the basis of autistic insensitivity to pain, suggested dysfunction of opiateergic systems, and others have confirmed elevated levels of opiate activity in cerebrospinal fluid and urine of individuals with autism (Gillberg, et al., 1996). This excessive opiate activity is thought to be responsible not only for a diminished sensitivity to pain, but also for symptoms like self-injurious and stereotypic behavior, social withdrawal, inability to convey emotions, reduced crying, attentional dysfunctions, labile affect, and aggressiveness (Panksepp, 1979).

All of the neuropathological arguments come with some supporting evidence and some conflicting, but none is yet conclusive. Of the data accumulated so far, the most extensive and consistent relate to the cerebellum and the limbic system. Theories regarding these structures have support from neuropathological, anatomical, physiological and behavioral studies (Bachevalier, 1994; Courchesne, Hesselink, Jernigan, Yeung-Courchesne, 1987; Ornitz, 1983; Ritvo, Freeman, Scheibel, Duong, Robinson, Guthrie, & Ritvo, 1986; Townsend, Courchesne, & Egaas, 1996). Discussion continues, however, and more studies must be done before any concrete conclusions can be drawn.
Evaluation

When evaluating autistic disorder, the clinician should assess the individual’s behavior and cognition in the areas of (1) social interaction, (2) communication, and (3) patterns of behavior, interests, and activities (APA, 1994). Impairment in any of these three areas can be extremely subtle, markedly apparent, or anywhere in between. In the area of social interaction, the clinician should assess the individual's use of nonverbal behaviors when interacting with others. Individuals with autism may show deficits in the use of eye contact, facial expression, gestures, or other nonverbal behaviors when interacting with other people. A lack of development of peer relationships is frequently present, and may range from having no interest at all in socializing with others to having an interest but not having the skills necessary to socialize (Kanner, 1943). Many individuals with autism do not share their enjoyment, interests, or achievements with other people. For example, a typically developing young child who sees an airplane fly overhead might point it out to his or her parents with delight, whereas the young child with autism is unlikely to try to draw attention to something of interest. Finally, deficits in social interaction might be manifested by a general lack of social or emotional reciprocity with others. For example, an individual with autism might not be sensitive to the feelings and emotions exhibited or expressed by other people.

The second major area assessed by the clinician is communication. Individuals with autism typically show a delay or lack of development of spoken language. They may lead others by the hand to desired items, but they usually do not compensate for their lack of spoken language through alternative forms of communication, such as the use of gestures. Individuals who do develop some speech typically show unusual speech patterns, such as immediate or delayed imitation of phrases that they have heard (referred to as "echolalia"), and frequent repetition of words or phrases that may have no communicative intent (Allen, 1988). Some individuals with autism develop a considerable amount of speech, but lack the skills necessary to initiate or sustain a social conversation. Finally, individuals with autism typically show a lack of variety of spontaneous "make-believe" play or social imitative play; when play skills are present, play tends to be more solitary, "concrete", and repetitive.

The third major area assessed is the individual's overall patterns of behavior, interests, and activities. Individuals with autism usually have a relatively limited repertoire of interests and activities, characterized by repetitive behaviors and frequent adherence to routines. Some individuals with autism show a preoccupation with one or several repetitive behaviors, such as lining up objects, collecting useless items, or have an unusually intense interest in a particular topic, such as trains or elevators. Insistence on following seemingly trivial routines may also be present. For example, an individual with autism might become very upset if there is a sudden change in a scheduled activity, if asked to sit at a different desk in school, or if a piece of furniture is out of place. People with autism frequently exhibit repetitive body movements, which are often referred to as "stereotypical" or "self-stimulatory" behaviors. These include, but are not
limited to, rocking, arm-flapping, hand and finger movements, body-posturing, and other unusual mannerisms. Finally, individuals with autism may show unusual attachments to objects (e.g., carrying around a wooden spoon), and/or preoccupations with objects or parts of objects (e.g., fascination with doorknobs).

To aid in the diagnosis of the above criterion behaviors, numerous observational scales have been constructed, but few of which are considered “gold standards”. One of the most psychometrically sound and well researched of the scales, the Childhood Autism Rating Scale (CARS) developed by Schopler, Reichler, DeVellis, & Daly (1980), relies upon ratings of an individual’s behavior through direct observation using a trained rater or skilled clinician. Likert-type items compose the scoring content of 15 items and individual items range from one (i.e., behavior within normal limits) to four (i.e., severely abnormal behavior). The internal consistency of the scale appears adequate to be considered a valid measure, with Cronbach alphas ranging between .73 to .93 for the total score. Test-retest and interrater reliability is psychometrically sound, though some interrater reliability suffers when considering each of the subscales (r = .10 to .93) to the exclusion of the total score (r = .68 to .80). Estimates of the CARS concurrent validity have been consistently high across clinical ratings, independent clinical assessments, and in comparison with the Ritvo-Freeman Real Life Rating Scale (RLRS; Freeman, Ritvo, Yokota, & Ritvo, 1986); r = .84, r = .80, and r = .77, respectively.

Another scale of similar psychometric merit is the Autism Behavior Checklist (ABC; Krug, Arick, & Almond, 1979; Krug, et al., 1980). The ABC was originally designed to be completed by educational personnel, though it has been suggested that parental input may provide valuable assistance and should be used when possible. The scale consists of a series of 57 questions, which are grouped in five behavioral domains; sensory, relating, body/object use, language, and social. The items are scored on a weighted dichotomous (i.e., yes/no) basis, with the weighting criteria determined by a normative base of 1,049 previously administered and analyzed scales. The internal consistency for the ABC exceeds that of the CARS, for both total score and factor structure (r = .87, and r = .30 to .70, respectively). Unfortunately, the ABC suffers from relatively poor interrater reliability (r = .40), as determined by chance corrected agreement. Additional problems appear to arise in the ABC when applied to older or higher functioning individuals, with a high rate of false negatives when using the original cutoff scores (Volkmar, Cicchetti, Dykens, Sparrow, Leckman, & Cohen, 1988). This discrepancy could be corrected through the establishment of ABC normative criteria specific to the aforementioned groups.

Other measures with diagnostic applicability to autism and autistic-related behaviors, include; the Diagnostic Assessment for the Severely Handicapped, revision 2 (DASH-II; Matson, Baglio, Smirolato, Hamilton, & Packlowskyj, 1996), the Ritvo-Freeman Real Life Rating Scale (RLRS; Freeman, et al., 1986), the Behavioral Summarized Evaluation (BSE; Barthelemy, Adrien, Tanguay, Garreau, Fermanian, Roux, Sauvage, & Lelord, 1990), and the Autism Survey (Campbell, Reichele, & Van Bourgondien, 1996).
Various problems are posed for the above rating scales and checklists. First, and as alluded to earlier, autism is a relatively heterogeneous syndrome. Second, considerable change can occur over the course of development and the importance of an age factor must be emphasized (Parks, 1983). Third, assessment instruments in the area of developmental disabilities have typically employed some variant of a deviance model. And, finally, some instruments rely on parental reports, which are unreliable, particularly, when retrospective report is required. Until these considerations are given full precedence, the assessment of autism will remain as elusive as the nature of the disorder itself.

Conclusion

Of all the pervasive developmental disorders, autism is perhaps the most fascinating, the most mysterious, and the most telling—fascinating, because of its impact on absolutely every aspect of a individual's perception of and interaction with the surrounding world; mysterious, because of the complexity of the many interacting brain systems that it perturbs; telling, because it strikes at the social, cognitive, and linguistic abilities that seem, at least on the surface, so essential to one's very humanity. During the past few decades, the riddle of autism has begun to yield to advances in the study of autistic behavior and the biological foundations, which affect this behavior. The examination of brain and behavioral functions in individuals with autism continues to supply new information on the nature and etiology of this complex disorder, and in doing so, brings us closer to an understanding of what exactly it means to be autistic.
References


