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Background and history of autism in relation to vision care

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Abstract Although autism existed before 1943, it was Leo Kanner who is credited with the first detailed description of autistic behavior. Before Kanner's report, the behavior was generally known as childhood schizophrenia. He noted that the outstanding common feature of all the children was certain parental personalities, like obsessiveness and lack of warm-heartedness. Concurrent with Kanner's report and observations were those of Asperger in 1944. However, Asperger's report, in a German-language journal, was not brought to the forefront until the 1980s. The children described by Asperger had milder forms of behavior disorders than those described by Kanner, with the resulting diagnosis of autism broadened and blurred. The main features of the new autistic spectrum included a triad of developmental deficiencies: recognition, communication, and understanding. Regardless of whose research is read, autistic behavior is considered peculiar and difficult to treat. Early treatments included LSD, tranquilizers, and developmental remediation. A later treatment, which proved to be the most successful, is applied behavior analysis (ABA), an outgrowth of B.F. Skinner's conditioning research. The etiology of autism remains a puzzle to scientists, with the most likely hypothesis being a central nervous system dysfunction. With regard to vision, people with autism tend to have abnormal electroretinograms, deficient evoked visual potentials, and atypical opticokinetic nystagmus. Other than a higher than expected incidence of strabismus and oculomotor deficiencies, refractive and binocular vision status of people with autism have been reported to be within normal ranges. Accordingly, the most useful tests for a patient with the diagnosis of autism are those for oculomotor function, opticokinetic nystagmus, and strabismus. The optometrist, thereby, becomes a member of the team helping to diagnose and treat the visual sequelae of autism.
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In recent years there has been a dramatic increase in the prevalence of autism, of up to 472%.[1,2] Accordingly, it is important for the optometrist to be aware of the nature of autism—particularly its history, etiology, treatment, and relation to vision.

Unlike a physical disease like tuberculosis, in which the diagnosis can be made by identifying the bacteria *Mycobacterium tuberculosis*, the diagnosis of autism, as with other disorders of behavior, is open to some controversy. Before Kanner,[3] the unusual behaviors (now linked to autism) were diagnosed as childhood schizophrenia. With the inclusion of Asperger's report,[4] a milder form of Kanner's autism became known as Asperger syndrome. Later the terms *Autistic Spectrum Disorder* and *Pervasive Developmental Disorder Not Otherwise Specified* came into use.

With the inclusion of the additional diagnostic categories, the lines of diagnosis of autism became blurred. An example is found in Bishop's[5] comprehensive discussion of the difficulty in making a diagnosis: he described a 4-year-old boy who was evaluated for language and social development by a multidisciplinary group consisting of a pediatric neurologist, a psychologist, a child psychiatrist, and a speech therapist. In the absence of any neurological signs, the pediatric neurologist made the diagnosis of dysphasia. The psychologist made the diagnosis of autism because of

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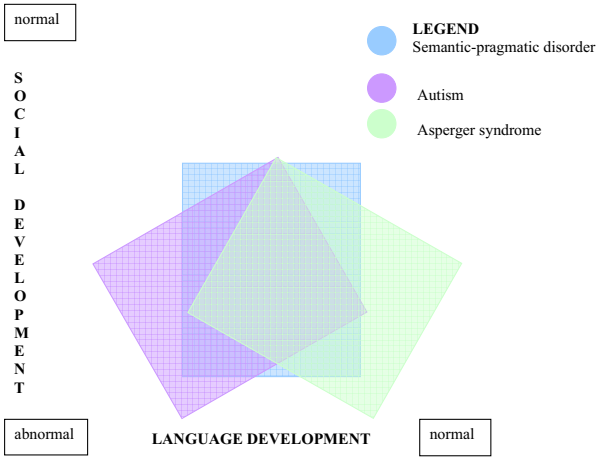

Figure 1 Diagnostic criteria diagram. The diagram graphically displays the difficulty with the overlapping diagnostic criteria among autism, Asperger syndrome, and semantic-pragmatic disorder, which are shown in the *gray*, *darker lavender*, and *darker green areas*, respectively.

poorly developed language and social behavior. A diagnosis of Asperger syndrome was made by the child psychiatrist because the child's language and social skills were not severe enough to make a diagnosis of autism. The speech therapist made a diagnosis of semantic-pragmatic disorder based on the child's poor conversational language skills. Finally, a visiting American pediatrician made a diagnosis of PDDNOS (Pervasive Developmental Disorder Not Otherwise Specified).

As noted in Figure 1, there is considerable overlap in the diagnostic criteria for autism, Asperger syndrome, and semantic-pragmatic disorder. This becomes a very important factor to the clinician, because, for example, all autistic patients will not be the same or even similar in some cases. In fact, there is a continuum as to the extent and severity of clinical signs that could be included under the diagnosis of autism. Perhaps one way to reduce some of the confusion in the diagnosis of autism is to trace the diagnostic criteria from that elaborated by Kanner[3] until today. Kanner's initial report on autism in 1943 listed 10 characteristics of autistic children and their families:

1. The primary and most noted sign is the child's inability to relate to others.
2. Mothers of these children report that the children did not show an anticipatory posture before being picked up.
3. Eight of the 11 children began speaking either on time or afterward.
4. Typically, the children had excellent memories.
5. The children demonstrated echolalia (repetition of particular sounds).
6. Words were interpreted literally.
7. Personal pronouns were used inaccurately.
8. The children had unusual reactions to sensory stimuli.
9. The children had the desire to keep the world around them constant.
10. All the children were from intelligent families.

Two characteristics require further explanation: characteristics 3 and 10. In 3, although language and communication skills are below normal for autistic children, Kanner may have been referring to the observation that the children's speech developed normally and was then lost with the onset of the autism. In 10, Kanner defined "intelligent family" as parents who were college-educated.

Broader criteria for the diagnosis of autism were introduced by Rutter[6] in these areas: (1) social development impairment, (2) faulty language development, (3) desire for sameness, and (4) onset before age 30 months. With the popularization of Asperger's work in 1981 by Wing,[7] Asperger syndrome became a term for a milder form of autism than that described by Kanner.[3]

The current diagnosis and definition of autism is given by the DSM classification, DSM-III-R and DSM-IV Autism Criteria. As opposed to a well-defined, finite set of signs and symptoms, the DSM classifications are a menu of possible inappropriate behaviors, thus clouding the lines between autism and other disorders of behavior. In other words, the original criteria for the diagnosis of autism described by Kanner have been broadened substantially with the addition of Asperger syndrome, Rutter's criteria, and the establishment of the diagnosis of autistic spectrum disorder.

Incidence

Because the criteria for diagnosis of autism are often varied, so are the rates of the incidence of autism as reported by Wing.[7] The range cited is from 1.2 to 16 per 10,000 in the United States, Europe, and Japan, and for the "autistic spectrum" as high as 47 per 10,000. A more current study reports that the recent changing criteria can result in an increase up to 28.8-fold[8] or an incidence of 1 in 150.

Etiology

As with the variability in the diagnosis and incidence of autism, there is also a wide variety of proposed etiologies. Perhaps the best way to illustrate this point is to take the proposed theories of one noted autism researcher and his coworkers. Edward Ritvo has been a distinguished and well-recognized researcher for more than 2 decades. The fact that he and his coworkers have failed to identify a definitive etiology of autism emphasizes and illustrates the elusive nature of the etiology. Below is a review of a sample of his publications from 1971 to 1992.

One of the conclusions of Kanner[3] (item 10), was that the parents of autistic children are intelligent. Following up on this theme, Ritvo et al.[9] conducted a survey, in 1971, with 148 families of autistic children. Compared with a matched group, no significant relationship was found to exist between autism and social class factors. Later in the 1970s, a theory relating autism to dysfunction of the vestibular mechanism was proposed. Freeman et al.[10] compared reinforcement of vestibular stimulation between autistic and

mentally retarded children. The reported results were that the reinforcing stimulation was more important to the autistic children than the comparison group. The data support an explanation for the typical self-stimulatory behavior of rocking in autistic children. An interpretation of the results by the investigators was that autism is related to central rather than peripheral neural mechanisms. In a related study, Tanguay et al.[11] compared REM (rapid eye movement) sleep activity between 16 autistic and 30 normal children. The comparison showed that autistic children, age 36 months to 62 months, had less discrete REM patterns than normal children, age 3 months to 68 months (see *EEG* below). Once again, Ritvo et al. attributed the difference to central nervous system mechanisms.

Another factor in the diagnosis of autism taken from Kanner's observations is repetitive behavior.[3] To investigate the mechanism(s) involved in repetitive behavior, Frankel et al.[12] measured the response of autistic children to photic stimulation compared with that of retarded children. Taking into account the results of a previous study,[10] the authors concluded that competition among various sources of reinforcement account, in part, for the autistic children's behavior.

In the 1980s there was a shift away from the vestibular connection with autism toward hematologic factors, which has led to today's concern about mercury and autism. One study in 1982 by Ritvo et al.[13] proposed exploring congenital, genetic, familial, and hematological factors. Ritvo et al.[14] reported on the autistic concordance of 40 pairs of twins who had met the study's guidelines. The data revealed concordance of 95.7% (22 of 23) for monozygotic twins, and 23.5% for dizygotic twins. A conclusion they made from these data is that there is a genetic component in the etiology of autism. One hematologic factor they found associated with autism is high levels of serotonin in the blood. Because the drug fenfluramine decreases serotonin, it was administered to 8 autistic patients.[15] Two of the patients showed a substantial improvement in academic and cognitive tests. In a later study exploring the cause of the hyperserotoninemia, Yuwiler et al.[16] measured the amount of serotonin antibodies in the blood of patients with childhood autism, schizophrenia, obsessive-compulsive disorder, Tourette's syndrome, and multiple sclerosis. The results showed that the elevated levels of serotonin were not caused by antibody activity.

By 1986, Ritvo[17] returned to the topic of the vestibular connection with autism. They examined the postmortem cerebella of autistic subjects and compared them with those of subjects without central nervous system impairment. The results showed a lower Purkinje cell count in the autistic subjects. (The Purkinje cell layer is the middle layer of the cerebellum's cortex, which is responsible for control on the body's motor function.) As an initial report with few subjects, no definitive conclusions regarding cause and effect were stated by the investigators. A later report using magnetic resonance imaging found no difference in midsagittal structures, such as the cerebellar vermis (which separates the 2 cerebellar hemispheres), between autistic and nonautistic subjects.[18]

The electroretinogram (ERG) began a new area of investigation by Ritvo and his coworkers into etiologic factors in autism. As with the hematologic studies, they were interested in genetic and hereditary factors related to the ERG in autistic subjects. A pilot study reported in 1989 failed to show any family factors in relation to autism and the ERG.[19] One year later (1990) Mason-Brothers et al.[20] reported on potential prenatal, perinatal, and postnatal factors in the etiology of autism by comparing autistic subjects with their nonautistic siblings. Once again, the role of genetics was not found to be an etiologic factor in autism as opposed to a conclusion from an earlier study.[14]

Although there are other theories pertaining to etiologic factors, they remain just that—theories. Certainly, Ritvo spent a great amount of time and effort and did not find any systematic etiology of autism. A general impression of Ritvo et al.[13] is that there is central nervous system involvement in the etiology of autism.

In a more recent review, Yazbak[21] cited other possible etiologies including mercury, more specifically, the preservative, thimerosal, used in the measles, mumps, rubella (MMR) vaccine. The relationship between mercury and autism has become a major controversy. A contemporary literature search on PubMed revealed 28 references using the search words *mercury*, *metabolism*, and *autism*. Examining the most relevant studies, it can be noted that some reports conclude a relationship,[22-26] including Rimland,[27] the noted authority on autism in his testimony before the U.S. House of Representatives. Others conclude that there is no relationship between autism and mercury,[28,29] including a very recent Fact Sheet from the Centers for Disease Control and Prevention.[30] There seem to be insufficient data to determine a specific etiology for autism.

Diagnostic adjuncts

Synesthesia

The uncommon and unusual phenomena of synesthesia may be defined as one sensory input being responded to by a different sense. For example, "seeing" a sound or "hearing" a color.[31] Although synesthesia was first recorded in the Old Testament[32] in the description of the Revelation at Mt. Sinai, more than 3,200 years ago, articles cite it as recently reported within the last 200 years.[33] Cytowic[34] states that 15% of people with autism experience synesthesia compared with 1% of the general population. The topic of synesthesia and autistic savants gained general popularity through the movie "Rain Man."[35] The explanation for these remarkable abilities of autistic savants was given by Luria in 1920.[36] Luria described a young man, whom he had studied for more than 30 years, with a memory that had "no distinct limits" as he could convert sounds into vivid visual

images. Once the sounds were visualized, the young man could repeat these long sequences forward or backward with equal ease. More recently, the absence of a corpus callosum and left brain abnormalities was given as a possible explanation for these unusual abilities of the well-known autistic savant, Kim Peek.[37]

Electrophysiology

Three areas of electrophysiologic study have particular relevance to the understanding of autism. The areas are electroencephalogram (EEG), ERG, and evoked potentials (EPs), especially the P300 wave of the EP.

Electroencephalogram. Asperger[38] stated that 80% of autistic children have anomalous EEGs. A high incidence of EEG abnormalities in low-performing autistic children was noted during the transition from being awake to being asleep.[39] In a related study, Tanguay et al.[11] found that autistic children have an immature REM sleep pattern. (The REM pattern of the EEG occurs during sleep, with oscillating eye movements associated with dreaming and dominant slow brain waves.[40]) A more recent study similarly found EEG abnormalities in autistic children.[41] More specifically, the abnormalities included alpha attenuation, hemispheric asymmetry, and increased slow wave activity. The consensus of opinion of the authors of these studies is that they suspect central nervous system involvement in the etiology of autism.

Electroretinogram. Simply stated, the ERG is the electrical response of the retina to light stimulation.[42] A combination of studies reported that the ERG in 49% of the patients with autism was abnormal[43] in contrast to 4.8% abnormal ERGs in the general population. The most probable etiology given for the abnormal ERG is faulty retinal physiology.[44]

Evoked potentials. In contrast to the EEG, which is a measure of the spontaneous electrical activity of the brain, EPs are electrical responses of the brain to sensory stimulation. The type of stimulation is typically either visual (VEP) or auditory (AEP).

One study in particular measured the VEPs in control subjects and subjects with autism while varying the stimulus onset asynchrony (SOA).[45] SOA is defined as the time differential between the presentations of 2 targets. For example, 2 visual stimuli, targets 1 and 2, are presented for 400 msec; target 1 is presented, and 150 msec later target 2 is presented for 400 msec. In this example, SOA is 150 msec. The purpose of measuring VEPs while varying SOA is to determine hemispheric processing. In this study, there was a difference in VEPs between control and autistic subjects. The author attributes the results to autistic people having a more general than specific reaction to spatial stimuli. Another experimental study also noted a reduced measured response in subjects with autism compared with subjects without autism.[46] In a comprehensive literature review, Ornitz[47] makes a similar comment regarding autism and problems of sensory processing.

P300. The P300 wave is a component of the EP, which occurs 300 msec after the onset of the stimulus, and is considered an index of cognitive functioning.[48] Studies indicate that the P300 wave is attenuated in children with autism.[49,50]

Opticokinetic nystagmus. Opticokinetic nystagmus (OKN) is one of the tests used clinically as a measure of visual acuity in preschool or nonverbal children.[51] Applying the OKN technique to autistic children, Scharre and Creedon[52] reported that only 3 of 34 subjects had a typical OKN response. Mestre et al.[53] reported similar results with autistic children, with only 6 of 22 subjects having a typical OKN. One conclusion for the possible reasons for the lack of an OKN response is either cerebellar or attentional disturbances.[52]

Vision disorders

Scharre and Creedon[52] measured visual acuity (using Teller Visual Acuity Cards), refractive error, binocular vision, and oculomotor status of people with autism. Binocular visual acuity ranged from 20/15 to 20/1600 with a mode of 20/80. Refractive error ranged from −4.25 to +3.25 diopters (D) with a median of plano. Astigmatism ranged from 0.25 to 3.25 with a mode of 1.50 D. Twenty-one percent of the children (7 of 34) were found to be strabismic, the majority having intermittent exotropia, compared with 3.7% incidence of strabismus for the normal population. The Lang stereotest was administered successfully to 47% (16 of 34) of the children, with 13 having a resolution of 550 seconds arc. Results of oculomotor testing were quite similar to the results of OKN testing, with only 5 of the 34 children who tracked the target.

In a study of oculomotor function of children with autism, Rosenhall et al.[54] reported that 6 of 11 (55%) of the subjects had saccades with undershooting and slow velocities. The cause for the faulty oculomotor function was speculated to be central nervous dysfunction with the possibility of physical brain damage.

One study, with 2 different investigations, noted an oculomotor relationship with autism, specifically, (1) children born to mothers who took thalidomide during pregnancy and (2) children with Möbius syndrome.[55] The common features noted in these children with autism were oculomotor disorders; no common cause for the findings was noted by the investigators; however, cerebellar dysfunction was suspected.

A likely explanation for the OKN responses and oculomotor disorders is provided by Belmonte,[45] whose theory involves attentional behavior of autistic children. More

specifically, based on electrophysiologic data from people with autism, there is evidence that they respond more physically generally than specifically to sensory stimuli.

Treatment

Kanner[3] recommended a special school for the children that he examined and described. The primary treatments for autism in subsequent years were pharmacologic in nature including LSD[56,57]and major tranquilizers.[58,59]

The major breakthrough in the treatment of people with autism was the application of behavior modification, known as ABA—applied behavior analysis.[60,61] ABA is an outgrowth of B.F. Skinner's reinforcement and conditioning research with animals.[62] Briefly, according to ABA, the method for modifying behavior is based on positive reinforcement, which increases a behavior; negative reinforcement, which decreases a behavior; and extinction, the withdrawal of reinforcement to decrease the rate of an undesirable behavior. Although negative reinforcement and extinction have the same result (a decrease in the rate of an undesirable behavior), extinction is preferred because negative reinforcement can lead to withdrawal and avoidance. Perhaps the most noted article in regard to therapy for children with autism was by Wolf et al.[63] The study reports on the successful training of Dicky, a 3.5-year-old boy, who was autistic and needed spectacles to correct his aphakia. (Incidentally, aphakia and autism are not usually related.) The ABA program targeted temper tantrums, bedtime problems, eyeglass wearing, eyeglass throwing, verbal behavior, and eating problems. For example, wearing eyeglasses was positively reinforced, and extinction was used to decrease tantrum behavior. After 3 months of hospital-based treatment, Dicky was discharged and returned home to his parents. After being home from the hospital for 6 months, Dicky's mother reported that he had been wearing his eyeglasses, no longer had tantrums or sleeping problems, was becoming more verbal, and had brought joy into the home.[63] During the following decades, ABA programs have been developed and expanded to become the treatment of choice for autism. Another of the pioneers, Dr. O. Ivar Lovaas, succinctly described the essential elements in a successful ABA treatment, which include a goal-oriented treatment plan, a competent therapist, and an ongoing evaluation to assess the status of the treatment program.[64]

Conclusion

While reviewing the literature pertaining to autism for the last 60 years, it seems that there are many unanswered questions. In particular, the factors that remain uncertain are etiology, diagnosis, and prevention.

A probable hypothesis is that autistic behavior is caused by a central nervous system dysfunction. This dysfunction involves the sensory systems, i.e., vestibular, auditory, and visual, and may explain the high incidence of synesthesia and irregular EEGs, ERGs VEPs, and OKN in autistic subjects compared with those in nonautistic subjects. Additionally, these sensory dysfunctions help explain some autistic behaviors such as spinning and echolalia.

The current review should help the clinician in several areas. Because of the wide range of behaviors in the diagnosis of autism, a patient with autism can be fairly high functioning; a socially withdrawn, nonverbal, and self-destructive individual; or anyone in between. Certainly, the lower the function of the patient, the more problems will be noted in electrophysiologic findings, oculomotor findings, OKN, and binocular vision status, specifically with respect to strabismus.[44,45,47,54] After reviewing selected references, it seems that OKN may be one of the tests in the evaluation of patients with autism. One may hypothesize that an autistic patient for whom OKN can be assessed is most probably high functioning and independent of overt behaviors, whereas when assessment is not possible, the child is most likely low functioning in general. Accordingly, the clinician can provide information to parents, educators, and psychologists about the patient's visual status and remedial options that might impact the patient's future activities both scholastically and with regard to activities of daily living.

The growing population of people with autism makes it very likely that optometrists will be examining more and more children with autism. With this, future study and activity should be devoted to developing a standard protocol for this unique population, optimizing visual function, and evaluating vision training techniques that increase intersensory integration.

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