Title Assessment of Autism in Children with Vision Impairment

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Running foot: AUTISM AND VISION IMPAIRMENT

Abstract

Aim: This study examined the utility of standard autism diagnostic measures in nine children (ages 5-9 years) with severe vision impairment and a range of social and language functioning.
Method: The Autism Diagnostic Observation Schedule (ADOS) and Autism Diagnostic Interview-Revised (ADI-R) were systematically modified and used to assess autism symptoms in children with severe vision impairment.Results of the assessments, including analysis of symptom patterns, were compared to expert autism diagnosis.
Results: Modified autism measures demonstrated good agreement with clinical diagnosis. Symptoms found to be most and least reliable in discriminating autism from behaviors common to most children with congenital vision impairment are described.Comparisons of current behavior and parent-reported behaviors from a younger age suggested that some symptoms of autism in very young children who are congenitally blind may improve with age.
Interpretation: The ADOS and ADI-R are useful for clinical assessment and to advance research efforts to understand autism symptoms in children with vision impairment. However, some autistic symptoms in very young children may change over time, and developmental changes should be closely monitored.

What this paper adds:

- Utility of modified autism measures in children with VI
- Analysis of autism symptom patterns in congenital severe VI
- Developmental changes in children with congenital severe VI

Symptoms suggestive of autism are often described in children with congenital vision impairment (VI). Keeler[1]first described autistic characteristics in five children with retinopathy of prematurity; similar reports have been described over the past fifty years.[2-6] Fraiberg used the term "blindisms" to describe repetitive, stereotyped behaviors common in congenitally blind children, such as eye-rubbing, hand movements (flapping, posturing), rocking, and rhythmic swaying.[4] Brown et al. described autistic features prevalent in congenitally blind children, including: atypical exploration of new objects (touch, smell), pronoun reversal, limited imaginative play, and self-stimulatory motor behaviors.[2] Clinicians and researchers have debated to what extent these characteristics can be attributed solely to congenital vision impairment versus indicating an autism diagnosis.[7,8] Research addressing the prevalence and developmental course of autism symptoms in children with congenital VI has been hampered by the lack of reliable and valid measures for assessing autism in this population.

Guidelines for autism intervention advise beginning treatment as early as possible,[9] yet often, children with VI who also have autism have difficulty obtaining a comprehensive clinical assessment and appropriate services.[10] It is essential to identify and validate autism diagnostic tools so that clinicians can accurately diagnose autism in children with VI and initiate appropriate interventions.

Investigators and clinicians have independently modified existing autism measures when assessing children with VI. Modifications exclude items specific to visual responsiveness and adjust cut-off scores in the Childhood Autism Rating Scale,[2,11-14]Autism Behavior Checklist,[14]and Social Responsiveness Scale.[15]However, the validity of modifications has not been tested, and they only address items that are directly vision dependent (e.g. eye contact) and not behaviors that may be an indirect result of VI.One published study of autism and VI used retrospective chart data including the Autism Diagnostic Interview – Revised (ADI-R),[16] but without information about whether modifications were made, or specific findings about the ADI-R symptom profile of children with VI with and without autism.[10] No published studies of children with VI have used the "gold standard" observational measure, the Autism Diagnostic Observation Schedule (ADOS; ADOS-2).[17,18]

This pilot study systematically tested the utility of autism diagnostic measures in children with severe VI with a range of social and language functioning.The objectives were (a) to determine if clinicians can reliably diagnose autism in children with severe VI using modified ADOS and ADI-R measures, (b) to identify specific items on diagnostic measures that correspond with a clinical diagnosis of autism, and (c) to identify symptoms that may be common in all or most children with severe VI and therefore are less useful in diagnosing autism in this population.

Methods

Participants

Nine children ages 5 to 9 years with severe VI were recruited between May 2009 and September 2011 by a neuro-ophthalmologist at a major children's hospital, where all data were collected. Inclusion criteria included best-corrected visual acuity of 20/800 (meaning the ability to see at 20 feet what a person with typical vision can see at 800 feet) or worse, and English-speaking. For children with limited communication, vision was assessed behaviorally based on fixation and pursuit of toys or light. In order to have an adequate sample to test the autism measures, the investigators purposefully selected patients from a practice in which most of the blind children have optic nerve hypoplasia (ONH), a condition felt to predispose to autism.[10] Seven children were congenitally blind due to ONH. One child developed optic atrophy

following an infection at age four years. Another child developed VI at age five years due to a head trauma that led to subretinal hemorrhages, retinal gliosis, and cataract. Participant characteristics are presented in Table 1.

[Table 1]

Measures

Autism Diagnostic Observation Schedule:[17] The ADOS is a semi-structured, standardized observational assessment of communication, social interaction, and play. Following consultation with experts on children with VI and approval from the publisher specific modifications were made:

(a) Free Play: added toys with interesting sounds and textures to the standard set.
(b) Construction Task: substituted an inset shape puzzle for the standard puzzle.
(c) Description of Picture: substituted a zoo scene with raised and textured piecesfor the standard picture. The assessor named each animal as the child felt it, then used the standard ADOS prompts to ask the child to tell about the animals.
(d) Tell Story from Book: substituted a Braille children's book[19] for the standard book.

The ADOS-2[18] was published after the children were assessed. It is functionally equivalentto the ADOSexcept for updated diagnostic algorithms; codes were transposed onto the ADOS-2 algorithms to compare algorithms for use with this population.

Autism Diagnostic Interview – Revised:[16] The ADI-R is a semi-structured, comprehensive diagnostic interview conducted with a parent or caregiver, focused on communication, reciprocal social interactions, and repetitive and stereotyped behaviors/interests. It includes symptoms occurring in the present as well as retrospective report of symptoms at age four years. Following consultation with experts on children with VI and approval from the publisher specific modifications were made:

(a) Onset of symptoms: focused on symptoms other than VI (developmental, communication, or social concerns).
(b) Items involving vision: deletedreferences to vision but retained examples related to other sensory modalities, or modifiedquestions to fit children with VI (e.g. change: "what does s/he do if someone else smiles at her/him?" to "what does s/he do if someone says something nice to her/him?").

Fourteen ADI-R items were modified; specific details are available in electronic supporting materials. Changes in scoring procedures for ADOS and ADI-R are discussed under Procedures.

Language phase: The ADOS was videotaped and transcribed. Mean length of utterance and additional information about language on the ADOS was used to determine language phase, following procedures outlined in Tager-Flusberg et al.[20] This rating provided an estimate of developmental functioning.

Procedures

Ethical approval for this study was provided by the Committee on Clinical Investigations (IRB). After obtaining informed consent, the modified ADOS and ADI-R were administered by the first author, a licensed psychologist with research certification in both measures. The first and third authors independently watched videotapes of the ADOS and ADI-R and determined whether each child met diagnostic criteria for an autism spectrum disorder; consensus diagnosis was reached if the psychologists initially disagreed on diagnosis. Both psychologists have extensive clinical experience in the assessment and diagnosis of autism and are research-certified in the ADOS.

The ADOS was scored using standard procedures except the following codes ("0" indicates non-autistic behavior):

(a) Unusual Eye Contact and Integration of Gaze and Other Behaviors during Social Overtures: scored "N/A;" coded "0" on algorithm.
(b) Responsive Social Smile: scored "0" if the child smiled when the assessor talked to the child in a friendly manner that did not imply physical touching.
(c) Response to Name: scored "0" if the child paused and clearly oriented to the assessor (e.g. turning head or saying "what?"); eye contact was not required.
(d) The following codes were scored "0" if all criteria for "0" were met except integration of eye contact: Pointing; Requesting; Showing; Spontaneous Initiation of Joint Attention; Language Production and Linked Nonverbal Communication.
(e) Response to Joint Attention: scored"0" if the child responded to the assessor's verbal cue, "Look at that!" by orienting or verbalizing in an attempt to identify the object being referenced.
(f) Unusual Sensory Interest in PlayMaterial/Person:close visual examination or tactual exploration (using the hands) to identify an object were not coded as unusual sensory interests.

The ADI-R was scored using standard procedures except the following codes:

(a) Direct Gaze: scored "N/A;" coded "0" in algorithm.
(b) Social Smiling: scored "0" if the child smiled in response to friendly verbalizations from others.
(c) Pointing: scored "0" if the child pointed to express interest; eye contact not required.

Results

Expressive Language Level

Two children were rated as language phase 1 (Preverbal Communication), two children language phase 3 (Word Combinations), and five children language phase 4 (Sentences). Since all the children were at least five years old, at least 44% of the sample was functioning below age expectations in expressive language skills.

Clinical Autism Diagnosis Reliability

The two clinicians agreed on seven of the children's diagnoses (agreement rate 78%; Kappa = .55). In two cases, one clinician diagnosed Pervasive Developmental Disorder Not Otherwise Specified (PDD NOS), and the other clinician diagnosed no ASD. The consensus diagnosis was no ASD in one case, and in the other PDD NOS.

Relationship between Scores on Diagnostic Tools and Clinical Autism Diagnosis

Scores on the diagnostic measures were compared to the clinical diagnosis; see Tables 2 and 3 for results.The ADOS classification using the original algorithm (with modifications described above) matched the clinician diagnosis in all cases.Using the ADOS-2 algorithm, one child who did not have ASD clinical diagnosis scored above the ADOS-2 autism cutoff.

[Table 2 and Table 3]

The ADI-R classification, using the standard diagnostic algorithm focused on symptoms at age four years, with the modifications described above, matched the clinician diagnosis in five out of nine cases (56% agreement; Kappa = .14). Three parents reported marked improvement in their children's social communication and engagement after age 5. Using the Current Behavior score on the ADI-R and comparing it to the cutoffs for the Diagnostic Algorithm, ADI-R classification matched clinician diagnosis in eight out of nine cases (89% agreement; Kappa =

.77). The following behaviors were abnormal based on parent report at age four in all three children with congenital VI who were *not* diagnosed with ASD, but were *not* abnormal in the non-congenital VI group: reciprocal conversation, nodding head for "yes," shaking head for "no," spontaneous imitation of actions, imaginative play with peers, range of facial expressions, initiation of appropriate activities, group play with peers, social disinhibition, circumscribed interests, repetitive use of objects or parts of objects, unusual sensory interests, hand and finger mannerisms, and other complex mannerisms.

Individual scoring codes were reviewed to determine which items best discriminated between children with and without a clinical diagnosis of ASD. Codes were considered to discriminate well if 75% or more of the children diagnosed with autism had a "1," "2," or "3" score, and almost all children with no ASD diagnosis scored "0". Codes were considered to have poor discriminationif 80% or more of the children with *no* ASD scored "1," "2," or "3". Table 4 presents the individual items with "good" and "poor" discrimination for ADOS and ADI-R current behavior.

[Table 4]

Discussion

This pilot study provides preliminary evidence in support of the clinical utility of the ADOS and ADI-R in the evaluation of children with severe vision impairment. This data suggests specific symptoms that may be more reliable than others in discriminating autism from behaviors that may be common to all or most children with congenital VI. These findings contribute to the small literature on autism in children with VI by utilizing a prospective (rather than chart review) design, gold standard observational and interview diagnostic measures, and detailing modifications so findings can be replicated.

Experienced clinicians using slightly modified diagnostic tools demonstrated inter-rater reliability in the diagnosis of ASD in the majority of children assessed. Results of ADOS testing and current behavior ratings on the ADI-R corresponded closely with clinical diagnosis, although these were not independent since clinicians used ADOS and ADI-R results in reaching a diagnostic conclusion; this approach is similar to that used by Lord and colleagues in the original validation studies for the ADOS with sighted children.[21] Blindness did not prevent the children without ASD from demonstrating levels of social engagement and social communication during the ADOS that clearly distinguished them from children with ASD.

This study provides initial guidance regarding which symptoms may be most important in the diagnosis of autism in children with congenital severe VI. Findings indicate that some symptoms suggestive of autism in sighted children do not distinguish ASD versus non-ASD in children withVI. Clinicians should be cautious about giving clinical significance to characteristics that were common in all or almost all congenitally-blind children in the present study (thus showing limited specificity), such as repetitive or stereotyped finger or hand movements, repetitive interests or stereotyped behaviors, absence of pointing, limited range of facial expressions, undue sensitivity to noise, difficulty with imaginative playby parentreport, and difficulty establishing age-appropriate friendships. Some of these symptoms (especially stereotyped behaviors) have also been found in other studies to be common in most children with congenital VI .[2,4,22] Given the frequency of stereotyped behaviors in non-autistic children with VI, the revised ADOS-2 algorithms (which include stereotyped behaviors in the total score), may be less appropriate for children with VI than the original ADOS algorithm which excludes these behaviors from the total score.

On the other hand, there were many symptoms of autism that had more reliable clinical significance in this sample because they were *not* present in the children with VI who did not meet criteria for a clinical ASD diagnosis. Blind children in this age group *without* ASD were able to demonstrate appropriate responsiveness to social situations and appropriate social overtures such as shared enjoyment, offering comfort, and directing others' attention.There were problematic behaviors reported almost exclusively in the blind children with ASD, and not in those without ASD: aggression (toward family members and non-family members) and self-injury.

Another notable finding was that parents of several children with congenital vision impairment reported marked differences in their children's behavior prior to and after age five years, with more autistic symptoms at age four (the focus of the ADI-R interview) compared to present symptoms (at age six to nine years). As these children developed and became more comfortable fully exploring their environments, their reciprocal social and communicative behaviors increased dramatically, and their self-stimulatory and repetitive behaviors significantly decreased. Therefore, diagnoses of ASD in very young children with VI may be less reliable than in sighted children and may not persist over time. This observation is consistent with research by Hobson and Lee[13] who re-evaluated nine congenitally blind children (ages 5 to 9 years at initial examination) and their sighted controls, all of whom were initially diagnosed with autism. Eight years after the initial diagnosis, only one of the nine blind participants met criteria for autism while all seven of the sighted controls continued to meet criteria.Additional research is needed to follow children with congenital VI over time, with frequent assessments beginning in infancy, in order to identify common developmental trajectories in autistic symptoms. Measures such as those tested in this study would be especially helpful to allow delineation of changes in specific symptoms over time.

The participants who met criteria for an ASD all had a diagnosis of ONH with more severe VI and more language delay than those participants without autism. While we did not assess neurological findings in this population, the lower language level and inherent high risk of developmental delay associated with ONH infer cognitive impairment. Autism in children with VI is often noted to be associated with neurological impairment,[2,5,6] and our results appear to be consistent with those findings.

This is a preliminary study with a small sample size, and as such there are a number of limitations. The study does not attempt to determine the prevalence of ASD in children with severe VI. Participants were not randomly selected, but rather chosen intentionally so as to provide a sample with a range of reported autistic-like symptoms and levels of developmental functioning to better test the utility of the autism measures. This preliminary evaluation of the utility of the modified autism measures was a first step toward being able to conduct robust research regarding ASD prevalence in this population. Subsequent research is needed to validate the measures in a larger sample including children with a wider range of diagnoses and levels of VI. Our study suggests that such a study may lead to modified ADOS and ADI algorithms and cutoffs for children with severe VI.

All seven of the participants with congenital VI had ONH. ONH is rarely isolated to VI and usually involves a combination of neuroradiographic abnormalities, endocrinopathies and developmental delay. Therefore, findings from this study may not generalize to children with VI due to other diagnoses, although the data regarding the utility of the autism measures in children with severe VI are still applicable.

The two participants with later onset VI were also the only participants with a diagnosis other than ONH. Neither participant demonstrated autistic symptoms. The small number of participants with later onset VI precludes drawingconclusions regarding differences between congenital and non-congenital groups. Qualitative clinical observations about the children with later-onset VI, suggested that they (a) used objects more in their play than the congenital VI group, (b) oriented their face more toward the assessor when talking or listening, and (c) used gestures such as nodding the head for "yes" and shaking the head for "no," which were not observed in the children with congenital VI. These preliminary observations suggest that the ADOS may be useful in conducting studies using a much larger sample of children with congenital versus later-onset VI, matched for level of VI; such studies would be helpful to better understand the impact of early congenital blindness on the development of social interactions.

In summary, this study found that modified autism diagnostic measures, including observational and parent-interview measures,are useful in conducting diagnostic evaluations in children with severe VI. Clinicians should be cautious of diagnosing autism in very young children with VI, since it appears that symptoms may improve markedly over the course of development in at least some children. In addition, clinicians shouldbe aware that some behaviors seem to have poor specificity in children with congenital VI, since they are exhibited by so many children in this population. Nonetheless, the autism measures were useful in ruling out autism in those children with VI who had appropriate socially reciprocal interactions, and suggest a promising methodology for conducting more extensive studies about the prevalence and developmental course of autism symptoms in children with VI.

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Table 1
Characteristics of Participants

ID	Age	Gender	Ethnicity	Vision Diagnosis	Best Visual Acuity	Lang-uage Level	History
1	5	F	Latina	ONH	NLP	1	Congenital VI
2	5	M	Asian	ONH	LP	1	Congenital VI
3	5	F	Latina	ONH	NLP	3	Congenital VI
4	7	M	Latino	ONH	LP	3	Congenital VI
5	6	F	Latina	ONH	Inaccurate reach for 2 in. toy at 1 foot using both eyes; only LP in either eye individually	4	Congenital VI
6	9	M	Latino	ONH	LP in right eye; poor fixation on 6 in. toy at 1 foot in left eye	4	Congenital VI
7	7	F	African-American	ONH	LP in right eye; 1/800 with left eye	4	Congenital VI; child abuse/neglect up to age 5
8	5	M	Caucasian	Optic atrophy	20/1000 in right eye; LP in left eye	4	VI caused by infection at age 4
9	5	M	Latino	L: cataract R: retinal gliosis Both: subretinal hemorrhage	Motion Perception	4	VI caused by abuse/head trauma at age 5

Note: ONH = optic nerve hypoplasia, NLP = no light perception, LP = light perception only, VI = vision impairment

Table 2
Diagnostic Classifications by Child

ID	ASD Clinical Diagnosis	ADOS Classification	ADI-R Classification	ADI-R Current Behavior
1	Autism	Autism	Autism	Autism
2	Autism	Autism	Autism	Autism
3	PDD	PDD	PDD	PDD
4	PDD	Autism	No ASD	No ASD
5	No ASD	No ASD	PDD	No ASD
6	No ASD	No ASD (autism on ADOS-2 algorithm)	Autism	No ASD
7	No ASD	No ASD	Autism	No ASD
8	No ASD	No ASD	No ASD	No ASD
9	No ASD	No ASD	No ASD	No ASD

Note: ASD = autism spectrum disorder, PDD = pervasive developmental disorder, not otherwise specified, ADOS = Autism Diagnostic Observation Schedule, ADI-R = Autism Diagnostic Interview – Revised

Table 3
Sensitivity, Specificity, and Diagnostic Agreement of Measures

Measure	% Children with ASD Diagnosis Exceeding Cutoff	% Children with no ASD Scoring Below Cutoff	Agreement with clinical diagnosis	Kappa statistic
ADOS original algorithm	100%	100%	100%	1.0
ADOS-2 algorithm	100%	80%	89%	.77
ADI-R standard algorithm	75%	40%	56%	.14
ADI-R current behavior	75%	100%	89%	.77

Note: ADOS = Autism Diagnostic Observation Schedule, ADI-R = Autism Diagnostic Interview – Revised

Table 4
Correspondence of Clinical Diagnosis with Individual Items

Correspondence with Diagnosis	Autism Diagnostic Observation Schedule Item	% Children with ASD Diagnosis Score 1, 2, or 3	% Children with no ASD score 0
Good	Frequency of Vocalization Directed to Others (Module 1)/Amount of Social Overtures (Module 2)	75%	80%
Good	Shared Enjoyment in Interaction	75%	100%
Good	Response to Name	75%	100%
Good	Response to Joint Attention	100%	100%
Good	Quality of Social Overtures	100%	80%
Good	Imagination/Creativity	100%	100%
Poor	Stereotyped/Idiosyncratic Use of Words or Phrases	50%	20%
Poor	Pointing	100%	0%
Poor	Facial Expressions Directed Toward Others	100%	20%
Poor	Unusually Repetitive Interests or Stereotyped Behaviors	100%	0%
Correspondence with Diagnosis	Autism Diagnostic Interview - Revised Current Behavior Item	% Children with ASD Diagnosis Score 1, 2, or 3	% Children with no ASD score 0
Good	Spontaneous Imitation of Actions	100%	80%
Good	Imaginative Play with Peers	100%	80%
Good	Showing and Directing Attention	100%	80%
Good	Seeking to Share Enjoyment with Others	75%	100%
Good	Offering Comfort	75%	100%

Good	Appropriateness of Social Responses	75%	80%
Good	Response to Approaches of Other Children	75%	100%
Good	Abnormal, Idiosyncratic, Negative Response to Specific Sensory Stimuli	100%	80%
Good	Aggression Toward Caregivers or Family Members	75%	80%
Good	Self-injury	75%	80%
Poor	Imaginative Play	100%	20%
Poor	Friendships	100%	20%
Poor	Undue General Sensitivity to Noise	100%	20%