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Autistic-Like Behavior in CHARGE Syndrome

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Children with CHARGE syndrome frequently exhibit moderate to severe behavior difficulties, and are often diagnosed with obsessive-compulsive disorder, attention deficit disorder, Tourette syndrome, and autism. Hartshorne and Cypher (2004) surveyed parents of 100 children with CHARGE worldwide and confirmed the prevalence of behaviors that are associated with these disorders. They also found behaviors that could be described as typical of persons who are deafblind. The present study examined whether the autistic-like behaviors of children with CHARGE are more similar to those of children who are deafblind, to those of children who are autistic or are unique to CHARGE. Surveys including the Autism Behavior Checklist (ABC) were mailed to families of 204 children with CHARGE, and 160 usable surveys were returned (78%). Total scores on the ABC for children with CHARGE were significantly different from the norms for those with autism, and those who were deafblind. However, the variance for CHARGE was larger than for the normative groups, and 27.5% of those with CHARGE could be classified as autistic. The pattern of subscale scores for those with CHARGE differed from the other normative groups.

KEY WORDS: CHARGE; autism; deafblind; rubella; behavior

INTRODUCTION

Behavior problems, often described as "autistic-like," have emerged as a feature of CHARGE syndrome. However, there has been little investigation of these behaviors. Lewis and Lowther [2001] noted that by school age most of the medical problems for children with CHARGE are well managed. At this point concerns focus more on education and behavior. However, "There has been very little investigation into the behavioral aspects of CA, and this is an area that deserves careful research in the future" (p. 72).

According to Kates et al. [1981], autistic-like behaviors commonly accompany deafblindness. They list behaviors such as withdrawal, lack of affect, an inability or disinclination to relate to others, self-abuse, self-stimulation, and perseveration, as common among persons who are deafblind. Other autistic-like behaviors that have been associated with deafblindness include light gazing, spinning, and rocking [Lenske et al., 1980], stereotypy [Sisson et al., 1993], and social skills deficits [Van Hasselt et al., 1989]. Thus, individuals with deafblindness and with autism share many behaviors.

Kahn [1991] used the Behavior Rating Instrument for Autistic and other Atypical Children (BRIAAC) to examine differences between children with autism and deafblindness. Kahn found the most disturbed behavior in the deafblind group; and, within the deafblind group, those who had congenital rubella syndrome were the most disturbed. Significant differences for the total deafblind group from those with autism were found on subtests for vocalization, sound and speech reception, social responsiveness, and body movement. Differences were not significant on relationship, communication, drive for mastery, and psychobiological subscales. This study suggests that there are differences between children who are deafblind and those who are autistic, with more "pathology" among the deafblind, particularly those with rubella.

Van Dijk [1991] compared the performance of children with deafblindness due to rubella syndrome to the norms on the Autism Behavior Checklist (ABC). The ABC has norms for both autism and deafblind. He found scores very similar to the ABC deafblind norms, which follow a similar pattern to those with autism, but are lower, with the mean considerably below that needed for a diagnosis of autism. Only one of his 17 cases met the criteria for autism. Thus, although van Dijk also found differences between deafblind and autistic behavior, he found children who were deafblind with rubella were less disturbed than those with autism.

Many, but not all, individuals with CHARGE are deafblind. Denno and Bernstein [1997] compared seven students with CHARGE at Perkins School for the Blind with a control group at the school matched for age, sex, and functional level. The control group included five with rubella syndrome, one with infantile encephalitis, and one with multiple disorders due to prematurity. The main identified difference was in the area of compulsive behaviors, where the students with CHARGE displayed more compulsive behaviors, as well as more negative behaviors when staff redirected or interrupted their compulsive behavior. While these authors did not look at autistic-like behaviors specifically, their study suggests that there is something unique about the behavior of children with CHARGE when compared to other students who are deafblind.

Fernell et al. [1999] reported on three children with CHARGE, all of who had elevated scores on the Autism Diagnostic Interview, and met the DSM-IV criteria for autism. It is uncertain whether any of the cases could be classified as deafblind. The first two cases had hearing impairments, but were reported to have normal vision. The third case had visual impairment, but only mild hearing impairment. This suggests that the autistic-like behavior in CHARGE might not be totally attributable to dual-sensory impairment. Fernell et al. suggested that a neuroendocrine dysfunction in CHARGE might contribute to the autistic behavior.

Hartshorne and Cypher [2004] conducted a web-based survey regarding the behavior of children with CHARGE, and received 100 responses from the US (74%) and seven other countries. Included was a medical history and a list of 71 behaviors typical of the diagnostic categories most frequently

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reported anecdotally in children with CHARGE, including autism, attention deficit disorder, obsessive-compulsive disorder, and Tourette syndrome. The authors obtained the list of behaviors from experts in the diagnoses listed and from an expert on deafblindness. The findings of the survey supported the anecdotal reports. In addition, children who were classified as deafblind received significantly higher ratings on challenging behaviors, specifically tic, autistic, and deafblind behaviors.

The literature suggests that the behavior of children with CHARGE is different in some of its characteristics from children who are deafblind from other etiologies, and that children who are deafblind, while having autistic-like behavior, may differ from children with autism. The purpose of the present study was to look more closely at the autistic-like behaviors of children with CHARGE to see if they are similar to or distinct from those who are diagnosed with autism and deafblindness. What differences are there in the autistic-like behavior of persons with CHARGE as compared with those who are deafblind and those who are autistic? It was predicted that the mean scores on autistic-like behavior for children with CHARGE would fall between the means for those with autism and those who are deafblind, and that children with CHARGE would have a different pattern of sub-test scores.

MATERIALS AND METHODS

After approval by the Central Michigan University Institutional Review Board, a survey was mailed to the families of 204 children who have CHARGE, ages 3 and up. All families were on the mailing list of the CHARGE Syndrome Foundation. Thus the sample is not a specific clinical group, and likely to be quite heterogeneous, particularly given the variability that exists in CHARGE. The survey contained three instruments: a CHARGE medical history, a demographic form, and the ABC.

There were two different medical history forms. One hundred of the families were also being surveyed as a follow-up to a previous study [Salem-Hartshorne and Jacob, 2004]. The CHARGE characteristics of these children had already been obtained. Thus they were mailed an update questionnaire asking for current vision and hearing status, age of walking, and any changes that may have affected development. The families of the additional 104 children were requested to complete a form (based on one developed by Salem-Hartshorne and Jacob, 2004) asking for information regarding the various medical problems associated with CHARGE, length of hospital stay after birth, number of surgeries, and number of post-birth hospitalizations. In addition there were questions about hypoxia, brain scans, age of walking, status of vision and hearing.

The test publisher Pro-Ed provided the demographic form, in order that the data collected could be used as a part of a norming project for a new edition of the ABC. In addition to basic demographic information it asked for educational placement and disability/exceptionality status.

The ABC is a component of the Autism Screening Instrument for Educational Planning Second Edition [Krug et al., 1993]. The Checklist (ABC) consists of a list of 57 behaviors that are checked if present. These are then coded onto five scales (sensory, relating, body and object use, language, and social and self help) as well as a total score. Total scores of 68 and above are considered indicative of autism. Norms are also provided for normal, deafblind, severely mentally retarded, and severely emotionally disturbed. Psychometric studies support the use of the ABC as a screening instrument [Eaves et al., 2000]. This test was chosen for three reasons. First, it is relatively simple for parents to complete. Second, it includes norms for deafblind, which allowed testing of the prediction that scores for persons with CHARGE would fall between those for autism and deafblind. Third, there was no intention to utilize this instrument to diagnose autism, but only to have a sample of behavior that has been found to discriminate between those with autism and those without.

RESULTS

Surveys were returned by 166 participants (81%). Three of the children had died at a young age, two were not certain in their diagnosis, and one was not yet 3-years-old, and so the results of these six were not included in the analyses.

Of the 160 children with CHARGE included in the analysis, 53% were male, 47% female. Thirty-two states were represented, with the most (15, or 9%) from California. They were predominantly Caucasian (93%), with six Hispanic, two African-American, one Asian/Pacific Islander, and three of unknown racial/ethnic background. Ages ranged from 3 to 33, with a mean of 10.9 years (SD = 5.6). The percentage of children with the various CHARGE characteristics is shown in Table I.

The mean and standard deviations on the ABC for the sample, compared with the norms for autism and deafblind, are shown in Table II. The total score obtained for the children with CHARGE was 48.53, with a standard deviation of 30.12. This mean is considerably lower than that for the autistic norms, but higher than that for the deafblind norms. Tests of statistical significance found the mean for CHARGE to be significantly lower than that for autism, $t(330) = 10.23$, $P < 0.000$, and higher than that for deafblind, $t(258) = 2.43$, $P < 0.02$, confirming the prediction that the average score for those with CHARGE would fall between those with autism and those who were deafblind.

It is important to note that the standard deviation for CHARGE was considerably greater than that found for the other groups (and for any of the groups described in the Manual for the ABC [Krug et al., 1993]). Children with CHARGE are extremely variable in their behavior. The ABC scores ranged from 0 to 81. The ABC uses a cutoff score of 68 for classification as autistic. By this score, 27.5% of the children with CHARGE could be so classified.

Hartshorne and Cypher [2004] found age to be significantly correlated with the presence of challenging behaviors. In the present study, however, age was not significantly correlated with ABC scores ($r = 0.07$). Table II shows the mean scores for autistic, deafblind, and CHARGE in five age categories as well as correlation with numbers of medical

TABLE I. Medical Problems in the Sample

Condition	Percent (N = 160)
Delayed motor milestones	99
Coloboma	85
Frequent middle ear infections	81
Sensorineural hearing loss	81
Vestibular problems	80
Heart defect	80
Swallowing problems	79
Growth deficiency	74
Choanal atresia or stenosis	64
Genital hypoplasia	56
Facial palsy	48
Renal problems	36
Spine anomalies	33
Cleft lip or palate	29
Tracheoesophageal fistula	22
Hand anomalies	18
Abdominal defects	18

TABLE II. Mean Scores on the ABC by Age and Total and Correlation Between ABC for CHARGE and Medical Score

Age	Autism	Deafblind	CHARGE	Correlation with medical[a]
3–4	87	37	59 (N = 15)	r = 0.552; $P = 0.03$
5–7	73	40	48 (N = 35)	r = 0.327; $P = 0.05$
8–10	79	43	48 (N = 40)	r = 0.361; $P = 0.02$
11–14	75	44	32 (N = 26)	r = 0.353; $P = 0.08$
15–33	71	29	56 (N = 44)	r = 0.077; $P = 0.31$
Total	77 (N = 172)	41 (N = 100)	49 (N = 160)	r = 0.247; $P = 0.002$

[a]This is the correlation between scores on the ABC and the total number of medical problems identified by the respondents.

problems. Interpretation of differences in scores between age groups is hampered by the absence of information on number of participants in each age group and of standard deviations in the ABC Manual. However, it is evident that mean scores vary in a non-linear manner for the five age groups, that is, scores on the ABC do not either increase or decrease with age.

The highest average total score for those with CHARGE (59) was obtained by children in the youngest age group. This was the smallest group (N = 15), so this finding might be due to sampling error. However, it may also be in part a result of the difficult medical issues that tend to be highly prevalent during the first few years. In an attempt to address that question, correlations were calculated between ABC scores and length of hospital stay after birth, number of hospitalizations, and number of surgeries. This was done for the sample as a whole, as well as separately for the 15 children in the youngest age group (3–4 year old). For the combined sample, none of the correlations achieved significance. However, when the 3–4 year old group was considered separately, the number of surgeries was moderately correlated with ABC scores (r = 0.465). Due to the small sample size, this coefficient is only significant using a one-tailed test, which is justifiable given the directional hypothesis, $P = 0.04$, 1-tailed. None of these variables were significantly correlated with ABC scores for any of the other four age groups.

Another way to consider the impact of medical conditions is to construct a medical involvement scale by simply awarding a point to each of the medical conditions [Salem-Hartshorne and Jacob, 2004]. Hartshorne and Cypher [2004] found this scale to be significantly associated with autistic-like behavior and tics. In the present study the correlation was also significant with the ABC, r = 0.247, $P = 0.002$. The correlation was also significant for each of the three youngest age groups (Table II).

The age group 11–14 was the only one where the mean fell below that for deafblind. There are three possible explanations. One is sampling error. A second is a cohort effect, as this was most likely the first group to have received the diagnosis of CHARGE at a fairly young age, and be more likely to have received appropriate treatment, including communication intervention [Thelin and Fussner, this issue]. The third is that by the preteen years the children are better established in their educational program. In most cases the medical problems are far behind them, and the difficulties of adolescence (which is usually delayed in CHARGE), have not yet begun. The oldest age group (15–33) had a higher average score, which could be influenced by adolescence, but also due to the fact that their diagnosis was probably delayed, as CHARGE was very new when they were born. An uncertain or inaccurate diagnosis may have resulted in less than optimal medical care and educational placement.

Table III shows the subscale scores for those with CHARGE compared with those from the ABC norms for those who are autistic and those who are deafblind. The subscales on the ABC have varying numbers of items, and thus cannot be compared with each other by score. However, subscale scores can be compared across groups. The scores for CHARGE generally fall between those for autism and deafblind, with the exception of "relating," where the CHARGE group fell below deafblind. While the use of subscales on the ABC has been questioned [Wadden et al., 1991; Sturmey et al., 1992], they do provide another way to consider how the children with CHARGE differ from the other two groups.

On two of the subtests, sensory and body object use, the average scores for CHARGE are about halfway between those for autism and deafblind. The sensory items reflect unusual reactions to sensory stimulation, e.g., showing no startle response, or covering one's ears at many sounds. The body and object use items reflect stereotypical behaviors such as rocking and hand flapping.

On the language subtest, the CHARGE score is nearly identical to the deafblind sample. These are items that were typical of the autism sample, but not the deafblind, such as avoiding pronouns, echolalia, and repeating sounds and phrases. On the social and self-help subtest, the CHARGE scores are very similar to the autism group. These include items such as self-abuse, resistance to change, and temper tantrums.

The relating subtest is the one score that is below both of the other groups. This has to do with relating to social stimuli, and includes items such as avoiding eye contact, avoiding touch, and looking through others.

Age of walking has been found to be positively associated with the presence of challenging behaviors [Hartshorne and Cypher, 2004] and negatively associated with the adaptive behavior [Salem-Hartshorne and Jacob, in press]. In both cases, age of walking was derived from a category scale (where ages are grouped together) (Table IV). In the present study, the correlation between age of walking using these categories and ABC scores was 0.36 ($P = 0.000$). Children who walked at an older age had higher scores for autism.

While the scores for CHARGE generally fell between autism and deafblind, not all children with CHARGE are deafblind. We created a category of deafblind for all children who had a moderate or greater loss in both eyes and ears. The forty children classified as deafblind had an average ABC score of 65,

TABLE III. Mean Subtest Scores for Three Groups

Scale scores	Autistic (N = 172) mean (SD)	Deafblind (N = 100) mean (SD)	CHARGE (N = 160) mean (SD)
Sensory	12.67 (5.20)	7.23 (3.50)	9.89 (5.89)
Relating	23.99 (7.80)	13.53 (6.41)	9.43 (9.25)
Body/object use	15.79 (8.32)	6.75 (6.69)	11.04 (9.75)
Language	12.20 (6.80)	6.31 (3.89)	7.14 (5.60)
Social	12.80 (5.70)	7.59 (4.24)	11.03 (6.45)
Total score	77.49 (20.01)	41.43 (16.94)	48.53 (30.12)

TABLE IV. Age Walked

Age	N (percent)[a]
<18 months	7 (4.5)
18 months–3 years	65 (41.7)
3–5 years	57 (36.5)
6–7 years	10 (6.4)
>7 years	5 (3.2)
Not yet walking	12 (7.7)

[a]There were 156 responses to this question.

whereas those who were not deafblind had an average score of 43. The difference was significant, $t(158) = 4.13$, $P = 000$).

DISCUSSION

The present study confirms that children with CHARGE frequently demonstrate behaviors that are autistic-like in nature. It also demonstrates again that great variability exists within the population of children with CHARGE, specifically in the area of behavior. This study further suggests that the autistic-like behavior in children with CHARGE is different in several respects from that of children with a single diagnosis of autism or deafblind.

The incidence of autism has increased over the past several years, with some authors attributing the rise to heightened awareness and increased diagnostic work-ups [Kabot et al., 2003]. Furthermore, autism is now considered a spectrum disorder, with different children demonstrating different combinations of symptoms. This makes diagnosis an interesting challenge, as there is variability in the behavior of children with autism, as is also noted in CHARGE. Thus, distinguishing the behavior typical of CHARGE from what is typical of autism is not straightforward. Nevertheless, we found that scores for children with CHARGE on the social and self-help subscale were most similar to children with autism. These included problems with change, tantrums, preoccupation with the manipulation of inanimate objects, and the presence of "special abilities" in one area of development. The CHARGE sample was least like children with autism on the subscale of relating. The children with CHARGE tended to be more likely than those with autism to attend to social stimuli, be responsive to social cues, make eye contact and touch, and form friendships.

The children with CHARGE also differed from those in the deafblind norms in certain respects. They had higher scores on social and self help (as we have seen above), and on body and object use. The latter involves such behaviors as rocking, spinning, flapping, and engagement in rituals. The ABC Manual does not describe the deafblind sample. Nevertheless, the children with CHARGE were most like this group on the language subtest. In comparison with the autism sample, both the CHARGE and the deafblind sample were less likely to reverse pronouns, have atonal or arrhythmic speech, repeat statements over and over, or engage in echolalia. The children with CHARGE fell below the average for the deafblind group on the relating subtest.

A picture begins to emerge of children with CHARGE being (1) generally more socially engaging and having better language and communication skills than children who are autistic, (2) engaging in more sensory related behaviors and more rocking, whirling and flapping than others who are deafblind, and (3) being similar to those with autism in trying to cope with the stressful demands of their environment, such as changes in routine. This, in turn, causes them to attend more to inanimate objects, to withdraw, or even to lose control in the form of tantrums, biting, hitting, kicking, etc.

There has been speculation that the medical issues faced by children with CHARGE influence the development of their autistic-like behavior [Hartshorne and Cypher, 2004]. The results of this study show that an association between these is greatest during the younger years when the medical problems are most salient. We also found that age of walking was associated with ABC scores. Age of walking has been found to be associated with behaviors in CHARGE by others [van Dijk, 1991; Hartshorne and Cypher, 2004; Salem-Hartshorne and Jacob, in press; Thelin and Fussner, in press]. Salem-Hartshorne and Jacob (in press) provide a model and evidence that age of walking is more important than medical issues in predicting adaptive behavior scores in children with CHARGE. The importance of age of walking as a predictor of outcomes in CHARGE needs further investigation, but it is intriguing given its association with vestibular difficulties, medical issues, and the importance of being upright in learning to understand and cope with one's environment [Brown, in press].

Children with CHARGE are multi-sensory impaired [Brown, in press]. This makes understanding and coping with the world challenging. Our finding that those who were deafblind had more severe behavior than those who were not deafblind was not surprising, and replicated the findings of Hartshorne and Cypher [2004]. However, it is clear that the behavior of children with CHARGE cannot be attributed solely to deafblindness, because those who are deafblind had a profile very different from the deafblind norms on this measure.

There is much to learn about the sources of challenging behavior in CHARGE. What is not certain is to what extent these behaviors are attributable to sensory impairments, medical conditions, stress, or to autism. The patterns of scores found suggest that teachers and parents may want to focus some of their attention on helping children with CHARGE learn to cope with change and environmental stressors. The large variance in ABC scores suggests that these autistic-like behaviors are not inevitable with CHARGE, but they must be a focus of concern. Future research should examine the prevalence of autistic-like behavior in clinical samples of children with CHARGE using instruments with superior diagnostic power than the ABC. Whether children with CHARGE may also be autistic, or whether the behaviors should be attributed to other causes unique to CHARGE, is still an open question.

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