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Behavioral Features of CHARGE Syndrome (Hall–Hittner Syndrome) Comparison With Down Syndrome, Prader–Willi Syndrome, and Williams Syndrome

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CHARGE syndrome, or Hall–Hitner syndrome (HHS), has been delineated as a common syndrome that includes coloboma, choanal atresia, cranial nerve dysfunction (particularly asymmetric facial palsy and neurogenic swallowing problems), characteristic ear abnormalities, deafness with hypoplasia of the cochlea and semicircular canals, genital hypoplasia, and variable heart defects, orofacial clefting, tracheo-esophageal fistula, renal anomalies, thymic/parathyroid hypoplasia, spine anomalies, short broad neck with sloping shoulders, and characteristic facial features. We conducted behavioral and personality assessments in 14 boys with HHS syndrome aged 6–21 years, and compared their characteristics with similar data from 20 age-matched boys with Down syndrome (DS), 17 boys with Prader–Willi syndrome (PWS), and 16 boys with Williams syndrome (WS). We used the Reiss Profile of Fundamental Goals and Motivation Sensitivities, the Achenbach Child Behavior Checklist (CBCL), and the Aberrant Behavior Checklist (ABC). All 14 boys with HHS were legally deaf, and 10 of the 14 were also legally blind. In comparison these other syndromes, boys with HHS had behavior that resembled autistic spectrum disorder. They were socially withdrawn, lacked interest in social contact, and manifested reduced seeking of attention from others, with hyperactivity and a need to maintain order. Though the boys with HHS showed decreased social interaction, they were not as socially impaired as in classic autism. Their language was delayed due to dual sensory impairment, cranial nerve deficits, and chronic medical problems, but their language style was not abnormal (no echolalia or jargon, no scripted phrases, and no pronoun reversal). Boys with HSS appeared frustrated, but they were not aggressive, or at risk for delinquency, manifesting few stereotypic behaviors or unusual preoccupations. They did not have a restricted repertoire of activities and interests. Their behavioral features appeared to be due to dual sensory impairment affecting hearing and vision, rather than to primary autistic spectrum disorder, but successful remediation requires similar educational interventions, which are discussed herein.

KEY WORDS: coloboma; choanal atresia; ear anomalies; deafness; facial palsy; heart defect; CHARGE association; Hall–Hittner syndrome; behavior; autism; dual sensory impairment; deafness; blindness

INTRODUCTION

The Hall–Hittner syndrome (HHS) was first described in 1979 by dysmorphologist Bryan Hall in 17 children with multiple congenital anomalies, who were ascertained because of choanal atresia with associated characteristic ears that were small, low-set, and deformed. These findings were frequently associated with cardiac defects, ocular colobomata (usually retinal), deafness, hypogenitalism in males, facial palsy, and postnatal growth problems with developmental delay. Also in 1979, ophthalmologist, Helen Hittner described the same new syndrome in 10 children with colobomatous microphthalmia, congenital heart defects, developmental delay, facial palsy, pharyngeal incoordination or paralysis, and external ear abnormalities with associated hearing loss. In 1981, Pagon et al. ascertained and reported additional children with either choanal atresia or coloboma and associated characteristic malformations, and coined the acronym CHARGE association (**C**oloboma, **H**eart Defect, **A**tresia Choanae, **R**etarded Growth and Development, **G**enital Hypoplasia, **E**ar Anomalies/Deafness).

The further delineation of this multiple anomaly syndrome with an autosomal dominant genetic basis was accomplished in 1998, when Tellier et al. reported 47 new cases. They emphasized several particularly distinctive features, including asymmetric facial palsy, esophageal or laryngeal abnormalities, renal malformations, facial clefts, and brainstem dysfunction requiring complex neonatal management via

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nasogastric or gastrostomy feeding tubes, Nissen fundoplication, and tracheostomy. They also observed complete or partial semicircular canal hypoplasia on temporal bone CT scans in all 12 patients that were evaluated, along with specific facial dysmorphology, and significantly increased paternal age at the time of conception (suggesting a genetic pathogenesis). Within the group of children previously diagnosed with CHARGE association, there is clearly a subgroup with such distinctive clinical characteristics that they appear to manifest a recognizable syndrome, which has come to be called CHARGE syndrome, or more properly, Hall–Hittner syndrome [Graham, 2001]. This syndrome remains difficult to diagnose due to its characteristic asymmetric involvement, and it occurs with an estimated frequency of 1.3:10,000, making HHS a common cause of multiple congenital anomalies [Issekutz et al., 2004].

When children with HHS enter the educational system with their dual sensory impairments, they frequently manifest challenging behaviors that reflect the impact of their limited sensory inputs. This study seeks to characterize these behavioral features through comparison with other common syndromes using established behavioral and personality assessment measures. Appropriate management strategies are also suggested to assist with educational interventions.

METHODS

Subjects with HSS syndrome were ascertained through the International CHARGE Syndrome Support Group as well as through referrals from university-based geneticists, after review and approval of our solicitation letter and study protocol by the Cedars-Sinai Medical Center Institutional Review Board. Interested families were also recruited at national chapter meetings as well as through mailings and were invited to participate in an ongoing study on behavior and management. Their clinical histories and photographs were reviewed to validate their diagnosis, according to the criteria listed in Table I. The facial findings in 4 of these 14 boys with HHS are shown in Figure 1. These HHS boys ranged in age from 6 to 21 years (mean age 12.4 years), and because this study was part of a larger study of hypogonadal males with mental retardation, only males were included. Comparison groups of developmentally disabled boys in the same age range (Table II) were selected from a larger data set of persons with Williams syndrome (WS), Prader–Willi syndrome (PWS), and Down syndrome (DS), as has been described previously [Dykens and Kasari, 1997]. The subjects in these comparison groups were ascertained at parent support group meetings, after clinical geneticists had previously diagnosed them. These comparison groups included 16 WS boys (mean age 12.1 years), 17 PWS boys (mean age 12.9 years), and 20 DS boys (mean age 12.1 years).

Subjects were matched across groups on gender and age. Levels of mental retardation for WS, PWS, and DS were based on parental reports of previously administered intelligence tests and were consistent with formal studies of IQ and cognition in each of these disorders. Most subjects with WS had moderate levels of mental retardation, while most subjects with PWS and DS had milder levels of mental retardation. Current standardized cognitive tests are not normed for deaf-blind children; hence, many individuals with CHARGE have never been formally tested and comparisons between groups using such tests would not be valid.

TABLE I. Characteristics of Hall–Hittner Syndrome

	Includes	Frequency
Major criterion		
C = Coloboma	Coloboma of iris, retina, choroid, disc; microphthalmia	80%–90%
C = Choanal atresia	Unilateral/bilateral, membranous/bony, stenosis/atresia	50%–60%
C = Characteristic ear abnormalities	External ear (lop or cup shaped)	
	Middle ear (ossicular malformations, chronic serious otitis), Mixed deafness, with temporal bone anomalies resulting in cochlear duct and/or semicircular canal hypoplasia	90%
C = Cranial nerve dysfunction	I: Anosmia, VII: Facial palsy (unilateral or bilateral), VIII: Sensorineural deafness and vestibular problems, IX and/or X: Swallowing problems	70–90%
Minor criterion		
Genital hypoplasia	Males: Micropenis, cryptorchidism	
	Females: Hypoplastic labia	
	Both: Delayed, incomplete pubertal development	70%–90%
Developmental delay	Delayed motor milestones, hypotonia, MR	100%
Cardiovascular malformations	All types: usually conotruncal defects (esp. tetraology of Fallot with AV canal defects and aortic arch anomalies)	75%–85%
Growth deficiency	Short stature	70%
Orofacial cleft	Cleft lip and/or palate	15%–20%
Tracheoesophageal-fistula	Tracheoesophageal defects of all types	15%–20%
Distinctive face	Characteristic face	70%–80%
Occasional findings		
Thymic/parathyroid hypoplasia	DiGeorge sequence without chromosome 22q11 deletion	Rare
Renal anomalies	Dysgenesis, horseshoe/ectopic kidney, hydronephrosis	15%–25%
Hand anomalies	Polydactyly, ectrodactyly, thumb hypoplasia	Rare
	Altered palmar flexion creases	50%
General appearance	Webbed neck	Rare
	Sloping shoulders	Occasional
	Nipple anomalies (accessory or hypoplastic)	Rare
Abdominal defects	Omphalocele	Rare
	Umbilical hernia	15%
Spine anomalies	Scoliosis, hemivertebrae	Rare

AV, atrio-ventricular.

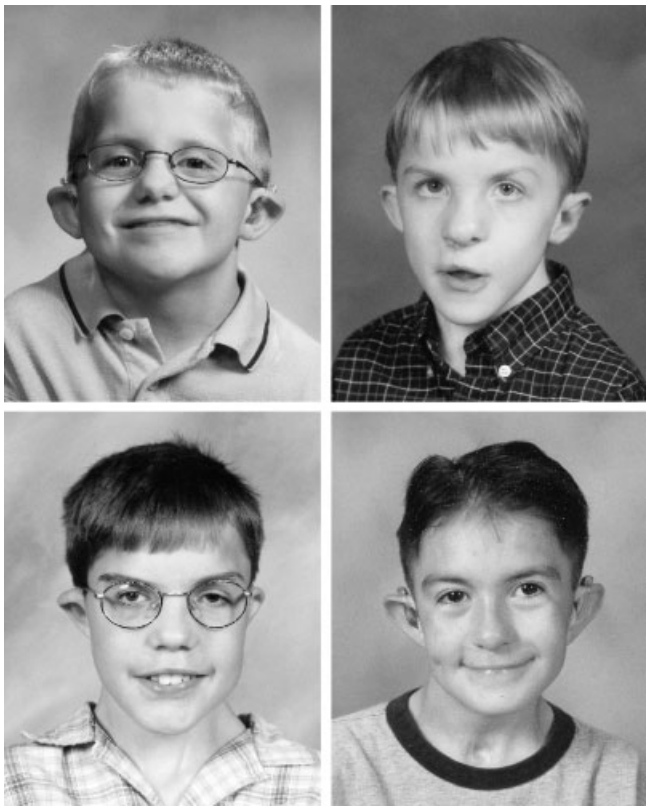

Fig. 1. Four unrelated children (**Top left**: age 7; **Top right**: age 7; **Bottom left**: age 13; **Bottom right**: age 13) with HHS who participated in this behavioral study and serve to demonstrate characteristic ear shapes and facial features for this condition. Note that although the underlying ear structure is similar and quite distinctive, even in the same child, the exact ear shape often varies significantly between the two sides, with typical changes including a triangular concha, small lobule, and extension of the antihelix toward the helical rim, where the lower helical fold is often thin or absent. The asymmetry of the facial palsy also results in characteristic facial asymmetry with a square shape in early childhood.

Parents were invited to participate in a study on the behavioral aspects of children with developmental disabilities. Parents of boys in each etiologic group completed the Child Behavior Checklist (CBCL) [Achenbach, 1991], Aberrant Behavior Checklist (ABC) [Aman and Singh, 1986], and the Reiss Personality Profiles [Reiss and Havercamp, 1998]. Data collected from these questionnaires were analyzed using means and variance to find the strengths and weaknesses of each group of boy's behavioral traits.

The CBCL utilizes a three-point scale (0 = not true; 1 = sometimes true; 2 = often true) to assess internalizing problems (withdrawn, somatic complaints, anxious/depressed), and externalizing problems (delinquent behavior and aggressive behavior). Other clinical domains include social problems, thought problems, attention problems, and other problems.

TABLE II. Participants

	N	Mean age	Age range
Hall–Hitner syndrome	14	12.40	6.00–20.92
Williams syndrome	16	13.32	5.91–31.62
Prader–Willi syndrome	17	12.89	6.39–26.91
Down syndrome	20	12.11	6.06–30.42

The CBCL has been widely used in both normal and clinical populations. The reliability and validity of this measure has been well established, and this instrument has also been successfully used in previous studies of persons with mental retardation. Data analyses used CBCL for the internalizing and externalizing domains, and total CBCL scores were also examined across groups.

The ABC consists of five empirically derived subscales encompassing 58 items that describe various behavior problems [Aman and Singh, 1986]. The subscales have been labeled: I, Irritability, Agitation, Crying (15 items); II, Lethargy, Social Withdrawn (16 items); III, Stereotypic Behavior (7 items); IV, Hyperactivity, Noncompliance (16 items); and V, Inappropriate Speech (4 items). The ABC is normed on persons with mental retardation, and has been used in many treatment outcome and descriptive studies of lower-functioning persons with mental retardation. The ABC thus complements data on maladaptive behaviors derived from the CBCL.

The Reiss Personality Profiles [Reiss and Havercamp, 1998] were available from parents of boys from each group. The Reiss Personality Profiles use a 5-point lichert scale (strongly disagree—strongly agree) to assess 100 questions about personality. The Reiss Profiles feature a 15-factor structure, which is consistent across people with and without mental retardation. The factor structure for persons with mental retardation was based on two studies of 950 participants that use factor analysis based on maximum likelihood extraction and confirmatory methods. The Reiss Profiles differ from many other available instruments for persons with mental retardation in that they do not measure maladaptive behavior or psychopathology, but instead assess motivational strengths and styles. Unusually high or low styles may, in turn, lead to aberrant behavior.

RESULTS

Examining the two domains of the CBCL, when compared with PWS boys, the boys with HHS had fewer internalizing behaviors and were less anxious and withdrawn, with fewer somatic complaints (Tables III and IV). Boys with HSS and PWS were more withdrawn than WS or DS, and HSS boys were less anxious than WS or PWS. DS boys had the least internalizing behaviors with low levels of withdrawal, somatic complaints, or anxiety. Scores for externalizing behaviors (aggressiveness and delinquency) were similar for HHS, DS, and WS, and significantly lower than those for PWS. PWS boys approached the clinical cut-point of 64 for problematic behavior in both domains, followed by HHS, WS, and DS. These HHS boys were not at increased risk for aggression or delinquency and appeared at low risk for maladaptive behaviors.

Mean scores for boys with HHS on the ABC were as follows: 1. Irritability, agitation = 9.00; 2. Lethargy, social withdrawal = 6.71; 3. Stereotypic behaviors = 5.21; 4. Hyperactivity = 8.93; and 5. Inappropriate speech = 2.00. Boys with HHS scored highest on irritability and hyperactivity, with moderately high scores on social withdrawal and stereotypic behaviors. The ABC is normed for persons with profound intellectual disability and so this measure was not utilized in this study for WS, PWS, and DS.

On the Reiss Personality Profile (Table V), HHS boys scored lower than DS, PWS and WS on social contact, and they manifested as much frustration as PWS boys, which was more than WS and DS. PWS and WS were more likely to seek attention than DS or HHS boys. As might be expected, PWS boys showed the most interest in food, followed by HHS, WS, and DS. HHS, WS, and DS all had similar activity levels, which exceeded those of PWS boys. HHS boys were most interested in maintaining order, followed by PWS, DS, and WS.

TABLE III. Mean Domains Raw Scores and SDs on the Child Behavior Checklist (CBCL) by group

	HHS		Williams		Prader–Willi		Down		
	M	SD	M	SD	M	SD	M	SD	*F*
Internalizing	7.36	6.39	6.50	7.26	12.18	11.03	3.78	3.28	3.73[a]
Externalizing	8.71	7.17	9.07	5.31	18.12	10.34	8.44	7.20	5.96[b]
Total CBCL	45.21	24.80	39.45	16.73	62.63	29.94	27.93	13.68	6.23[b]

[a]$P < 0.05$.
[b]$P < 0.001$.

DISCUSSION

History of CHARGE Association and HHS

A new multiple anomaly syndrome associated with choanal atresia and ocular colobomata was first reported in 1979 in separate publications by Hall [1979] and Hittner et al. [1979]. Hall described 17 children with small, low-set, deformed ears, cardiac defects, ocular colobomas (usually retinal), deafness, hypogenitalism in males, facial palsy, and postnatal growth problems with developmental delay. Hittner reported 10 children with colobomatous microphthalmia, congenital heart defects, developmental delay, facial palsy, pharyngeal incoordination or paralysis, and external ear abnormalities with associated hearing loss. In 1981, Pagon et al. further delineated this condition and first coined the acronym CHARGE association (**C**oloboma, **H**eart Defect, **A**tresia Choanae, **R**etarded Growth and Development, **G**enital Hypoplasia, **E**ar Anomalies/Deafness). In choosing this acronym, the intent was to emphasize that this clustering of associated malformations occurs more frequently together, than one would expect on the basis of chance, and that the etiology for the association between these defects was unknown. Early studies emphasized the occurrence of choanal atresia or ocular colobomata as key features in ascertaining children with this disorder. Since these features are not invariably present in all affected children, it took additional time and clinical observation to recognize the key importance of the characteristic ear and temporal bone morphology, as well as the characteristic cranial nerve dysfunction. Because these key findings are usually asymmetric, the facial phenotype of each individual patient is much more varied than typically seen in other syndromes. As time has gone on, most clinicians have come to recognize that HSS can also be a cause for syndromic cleft lip and/or cleft palate, and also for syndromic tracheo-esophageal fistula.

Over the past 20 years, the specificity of this pattern of malformations has now reached the level that many clinicians and most parents in the CHARGE Syndrome Support Group now consider HHS to be a discrete recognizable syndrome with a genetic basis. With increasing experience, it has become clear that the CHARGE association criteria originally proposed by Pagon et al. [1981], and later revised by Mitchell et al. [1985], needed further refinement. Revised consensus diagnostic criteria, incorporating both major and minor features for CHARGE, were set forth by Blake et al. [1998] and expanded by Graham [2001] and Amiel et al. [2001]. They suggested that these criteria (Table I) might ultimately define HHS as a recognizable syndrome within CHARGE association.

Major diagnostic criteria were those findings, which occurred commonly in CHARGE, but were relatively rare in other conditions: **c**oloboma, **c**hoanal atresia, **c**ranial nerve involvement (particularly asymmetric facial palsy and neurogenic swallowing problems), and **c**haracteristic ear abnormalities. These ear findings have been further revised to include both the distinctive asymmetrical auricular defects emphasized previously, as well as characteristic temporal bone anomalies [Amiel et al., 2001; Graham, 2001]. Hypoplasia of the cochlea (the Mondini malformation), with absence of the semicircular canals was first reported by Guyot et al. [1987] in temporal bone specimens from a child with CHARGE association. The uniqueness of these findings was subsequently confirmed through large series of temporal bone tomograms in the otolaryngology literature, where such findings are considered pathognomonic for HHS [summarized in Amiel et al., 2001]. Wiener-Vacher et al. [1999] documented that defective vestibular function was associated with absent semicircular canals in children with HHS, and suggested that their severe delays in psychomotor development were multifactoral due to vestibular impairment, auditory impairment, visual impairment and chronic medical problems. Amiel et al. [2001] confirmed that semicircular canal agenesis/hypoplasia was sufficiently frequent and distinctive in HHS to be included as a major diagnostic criterion.

Minor diagnostic criteria, which occur less frequently (or are less specific to CHARGE) include: heart defects, genital hypoplasia, orofacial clefting, tracheo-esophageal fistula, short

TABLE IV. Means, Standard Deviations, and *Fs* for the CBCL Subdomains Across Groups

	HHS		Williams		Prader–Willi		Down		
	M	SD	M	SD	M	SD	M	SD	*F*
Withdrawn	2.79	2.22	1.79	2.29	4.71	4.09	1.85	1.57	4.29[a]
Anxiety	2.43	3.20	3.80	4.92	4.71	5.54	1.37	1.64	2.29
Somatic	2.14	2.18	1.87	2.53	2.76	2.46	0.74	1.05	2.95[a]
Social	5.29	2.30	5.00	2.83	7.00	2.81	3.94	1.86	4.57[b]
Thought	3.50	2.10	2.00	2.07	3.50	2.00	1.35	1.57	5.46[b]
Attention	8.93	4.63	7.67	3.70	7.35	4.08	4.42	2.50	4.47[b]
Delinquent	1.29	1.64	2.07	1.14	4.65	3.67	1.65	1.69	7.31[c]
Aggressive	7.43	6.14	7.00	4.58	13.47	7.70	7.06	5.82	4.34[b]

[a]$P < 0.5$.
[b]$P < 0.01$.
[c]$P < 0.001$.

TABLE V. Means, Standard deviations, and *Fs* for Reiss Personality Profile Domains Across Groups

	HHS		Williams		Prader–Willi		Down		
	M	SD	M	SD	M	SD	M	SD	*F*
Activity	18.00	5.52	18.53	4.37	13.88	5.45	19.45	3.98	4.43[a]
Anxiety	12.73	4.10	12.73	4.06	12.56	3.95	11.65	2.94	.35
Attention	20.42	5.48	25.00	4.91	25.13	3.79	20.89	4.93	4.26[b]
Curiosity	31.92	5.82	27.93	4.74	28.00	3.98	27.85	4.64	2.43
Food	22.77	16.33	18.46	6.09	29.00	5.79	15.55	4.65	7.39[c]
Frustration	24.38	6.61	22.00	4.19	25.69	5.45	18.74	4.36	6.08[c]
Help Others	21.50	7.76	26.80	6.46	27.25	5.45	27.80	4.50	3.21[a]
Independence	18.77	3.79	19.20	4.35	22.60	5.46	21.26	3.80	2.45
Morality	12.00	4.31	12.00	3.46	13.24	1.89	12.60	2.56	0.58
Order	20.31	3.15	13.53	3.52	19.94	5.11	15.44	5.63	7.95[c]
Pain	12.42	5.74	18.13	4.19	14.00	4.02	11.89	4.41	5.97[c]
Rejection	20.46	6.78	24.33	4.91	24.56	6.36	19.95	5.84	2.73[a]
Sex	8.38	3.12	8.71	3.12	6.63	1.89	9.20	3.46	2.38
Social	23.77	5.20	28.33	3.54	25.19	3.41	24.50	4.17	3.59[b]
Vengeance	16.92	10.63	14.47	4.45	17.00	5.76	13.30	4.60	1.35

[a]$P < 0.5$.
[b]$P < 0.01$.
[c]$P < 0.001$.

stature, and developmental delay. Other occasional less-specific findings include: renal anomalies, thymic/parathyroid hypoplasia, hand and spine anomalies, webbed neck, sloping shoulders, nipple anomalies, characteristic facial features, and abdominal defects. When orofacial clefting is present, the choanae are usually patent, so this finding can substitute for choanal atresia, particularly if the remaining findings are otherwise characteristic for HHS. Individuals with all four major characteristics, or three major and three minor characteristics, unquestionably have HHS. Some of these features are difficult to detect in fetuses or neonates, therefore, the diagnosis needs to be considered in any infant with one or two major characteristics and several minor characteristics. Evaluation often requires directed evaluation for clinically less obvious features, including a cranial CT scan to look for abnormalities affecting the temporal bones, choanae, or brain, as well as echocardiography, renal ultrasonography, and retinal evaluation [Blake et al., 1998; Graham, 2001].

Most cases have been sporadic occurrences in an otherwise normal family. A teratogenic etiology for CHARGE association was initially suspected, but this has not been substantiated. A few families have manifested parent-to-child transmission and recurrences among siblings born to normal parents suggesting possible germ cell line mosaicism [Blake et al., 1998]. There has been concordance in affected monozygotic twins, discordance in dizygotic twins, and statistically advanced paternal age among sporadic cases of HSS, with paternal age 34 or greater noted in 43% of cases [Blake et al., 1998; Tellier et al., 1998]. Different chromosome alterations have been noted in a minority of patients with CHARGE association, suggesting the possibility of a submicroscopic chromosomal deletion, but two studies using comparative genomic hybridization or microsatellite markers failed to detect any microdeletions in patients with HSS [Sanlaville et al., 2002; Lalani et al., 2003]. Recently, Vissers et al. [2004] demonstrated chromosome 8q12 microdeletions by array comparative genomic hybridization in two individuals with HSS. Among the genes in this deletion, they subsequently detected mutations in the gene *CHD7* in 10 of 17 individuals with CHARGE syndrome who had no microdeletion. This suggests that HHS can result from haploinsufficiency for the CHD7 protein. This protein plays a pivotal role in early embryonic development by affecting chromatin structure and gene expression, and this gene is temporally and spatially expressed in the same developing tissues, which are affected in HSS [Vissers et al., 2004].

Developmental Trajectories of Children With HHS

Children with HHS usually manifest markedly delayed motor development, with many not achieving mobility by rolling, shuffling on their backs, or scooting until the average age of 20–25 months [Davenport et al., 1986]. The presence of upper body hypotonia may add to their truncal instability, and difficulties with balance further contribute to delays in walking. The average age of independent walking for children with HHS is 35–57 months, and those who shuffle on their backs usually walk later (average age 57 months). Children with HHS who crawl normally tend to walk at an average age of 35 months [Blake and Brown, 1993]. Older children may show continuing difficulties in maintaining their balance, especially on uneven surfaces. These motor difficulties result from vestibular dysfunction due to hypoplasia/aplasia of the semicircular canals, combined with visual field defects, decreased visual acuity, hearing impairment, truncal hypotonia, and the sequellae of chronic medical problems [Wiener-Vacher et al., 1999]. Thus, a thorough initial medical evaluation can suggest anatomic findings that will require specific developmental interventions that can begin in the neonatal period. Physical therapy to facilitate mobility can be extremely important, and early success in mobility is associated with improved developmental outcomes. Tactile defensiveness and oral aversion warrant intervention from an occupational therapist skilled in sensory integration.

Cognitive Functioning

Much of the early literature suggested that mental retardation was a constant feature of HHS, and though some children with HHS ultimately function within this range, many children do much better than their severe delays in early motor development might initially suggest [Goldson et al., 1986; Blake et al., 1990; Harvey et al., 1991; Blake et al., 1998]. Recently, other types of learning disability, such as communicative disorder, attention deficit disorder, pervasive developmental disorder, obsessive-compulsive disorder, and autism have been noted [Stromland et al., 2003; Smith et al., 2004].

The degree of early developmental delay may be a poor predictor of ultimate intellectual capabilities, since early intellectual assessments tend to look closely at gross and fine motor development, as well as speech skills. Later cognitive capabilities, once the child has developed an effective communicative system, and motor performance has improved, are often much better than expected [Goldson et al., 1986; Blake et al., 1990, 1998]. Lengthy hospital stays may result in limited developmental intervention during the early months. In later life there may be a lack of skilled developmental therapists, who are knowledgeable about educational services for children with multi-sensory impairment. These factors, combined with inadequate assessment techniques, may result in the diagnosis of severe to profound mental retardation or autism in older children with HSS.

Maladaptive Behavior in Children With HSS

Our study of 14 boys with HSS who were legally deaf, with 10 also legally blind, suggests that they manifest behavior that superficially resembles autistic spectrum disorder. When compared with PWS boys on the CBC, HHS boys had fewer internalizing behaviors and were less anxious and withdrawn, with fewer somatic complaints (Tables III and IV). Boys with HHS and PWS were more withdrawn than WS or DS, and DS boys had the lowest levels of withdrawal, somatic complaints, or anxiety. Scores for externalizing behaviors (aggressiveness and delinquency) were similar for HHS, DS and WS, and much lower than those for PWS. This suggests a low risk for aggression and delinquency, and boys with HHS appear at low risk for maladaptive behaviors. On the ABC boys with HHS scored highest on irritability and hyperactivity, with moderately high scores on social withdrawal and stereotypic behaviors.

On the Reiss Personality Profile (Table V), HHS boys scored lower than DS, PWS, and WS on social contact, and they manifested as much frustration as PWS boys, which was more than WS and DS. Boys with PWS and WS were more likely to seek attention, than boys with DS or HHS. As might be expected, PWS boys showed the most interest in food, followed by HHS, WS, and DS. Boys with HHS, WS, and DS all had similar activity levels, which exceeded those of boys with PWS. Boys with HHS were most interested in maintaining order, followed by PWS, DS, and WS.

Thus boys with HHS were socially withdrawn, lacked interest in social contact, and manifested reduced seeking of attention from others, with some hyperactivity and a need to maintain order. Their language was delayed due to dual sensory impairment, cranial nerve deficits, and chronic medical problems, but their language style was not abnormal (no echolalia, no scripted phrases, and no pronoun reversal). Boys with HSS were frustrated, but they were not aggressive, or at risk for delinquency, manifesting few stereotypic behaviors. They did not have a restricted repertoire of activities and interests. Our results suggest that boys with HHS have behavior that resembles autistic spectrum disorder, possibly due to dual sensory impairment affecting hearing and vision. It is important to appreciate the impact of their dual sensory impairment on communication, socialization, and behavior. We hope that our research will stimulate further investigations to examine the link between dual sensory impairment syndromes and autism spectrum disorders.

In contrast to HHS, individuals with PWS show a mix of compulsive behaviors (hoarding, ordering, redoing, and repetitive questioning), which can lead to tantrums, stubbornness, and controlling manipulative behavior, which is often food-oriented [Dykens and Kasari, 1997]. The boys with DS in this study had low levels of withdrawal, somatic complaints, and anxiety, though in other studies their anxiety and withdrawal tends to increase with age, leading to increased stubbornness and disobedience at older ages, with lowered activity levels and a preference for being left alone [Dykens and Kasari, 1997]. Behavior in WS is characterized by attention-deficit disorder, overfriendliness, and generalized anxiety. Thus WS, PWS, and HHS boys all manifested more anxiety than DS, and boys with PWS and WS were more likely to seek attention, than DS or HHS. Boys with HHS were most interested in maintaining order, probably because of their sensory deficits. Boys with HHS and PWS were also more withdrawn at this age than WS or DS, but boys with HHS remained curious and had a low risk for maladaptive behaviors.

Other studies in this Special Issue on CHARGE syndrome investigate behavior in persons with this syndrome. Preliminary evidence from CHARGE syndrome patients encountered through the Canadian Pediatric Surveillance Program who were old enough to be assessed for Autistic Spectrum Disorder also suggests an association between these disorders [Smith et al., 2004]. This association is further supported in a study by Hartshorne et al. [2004] in which scores on the Autism Behavior Checklist were equal to or greater than 68 (consistent with a diagnosis of autism) in 25% of 166 participants with CHARGE syndrome. For the group with CHARGE syndrome, their total score of 48.53 was much closer to the total score of 77.49 for the group with autism, than it was to the group with normal function (3.90), and similar to the Deaf-Blind group (41.43).

Salem-Hartschorne and Jacob [2004] examined changes in adaptive behavior scores over a 4-year-period in 100 individuals with CHARGE syndrome and noted that the age at walking, degree of hearing and visual impairment, and severity of medical involvement were negatively correlated with adaptive behavior scores. Thelin and Fussner [2004] underscored the importance of achieving early mobility in a study of 31 individuals with CHARGE syndrome whose parents were interviewed regarding the effects of medical problems, sensory disorders, and behavior on the development of communicative skills. These parents noted that inappropriate behavior was a consequence of poor communicative skills. The authors found that the development of symbolic language, and thereby the ability to achieve an effective means of communication and social interaction, was not related to the degree of vision loss, hearing loss or other medical problems. Instead, use of symbolic language was significantly related to two factors: ability to walk independently, and early use of total communication training throughout childhood.

European educators noted that over half of 71 children with CHARGE syndrome manifested hyperactivity, with difficulty in waiting, difficulty in understanding and using social rules, and pleasure in watching objects spin and in throwing objects [Souriau et al., 2004]. Difficulty in waiting their turn to speak was linked to difficulty in understanding and using social rules, as well as with taking pleasure in throwing objects. Over two thirds of these children needed help with temporal reference points, which required a structured environment that allowed the child to anticipate events. One fifth of these children were unusually anxious, and they tended to manifest aggression toward themselves and others.

Bernstein and Denno [2004] have confirmed these observations in a study of 29 students with CHARGE syndrome. These authors noted a high rate of repetitive behaviors (averaging 11.5 repetitive behaviors per student), which significantly interfered with their daily routines. These repetitive behaviors were challenging to treat, and 34% of these students responded to redirection with aggression toward themselves or others. Hence, different types of repetitive behaviors required different types of corrective techniques. Self-stimulatory behaviors were treated with sensory motor integration, teaching other new behaviors, or by using harmless behaviors as reinforcers. Maladaptive behaviors were treated by changing the environ-

ment to disrupt the routine, reinforcing flexibility, and replacement with adaptive behaviors. Tics were treated by giving the movement a name and allowing the student time to tic, and by teaching coping strategies, while educating the student regarding the social consequences of the behavior. Obsessive compulsive behaviors were treated with redirection and teaching internal controls.

Executive function skills are needed to control and regulate organized behavior and cognition through sustained attention and memory. Impaired executive function can result in impulsivity and disinhibition, impaired judgment and self-awareness, and difficulties in making mental or behavioral shifts, especially in new situations or with new tasks. One case report of a 12-year-old girl with CHARGE syndrome confirmed deficits in executive function that resulted in her manifesting inattention and disorganization, which hampered her memory despite normal non-verbal and tactual/spatial problem-solving skills [Nicholas, 2004]. Because of this, she had problems understanding social situations, despite a strong desire to have friends, and she had academic difficulties due to inattention and disorganization. Remediation was accomplished through learning activities designed to promote flexible, strategic and organized problem-solving skills, and the use of a self-report diary to promote self-monitoring and emotional control. A second approach was to focus on classroom accommodations to promote sustained attention and increase communicative skills.

Educational Intervention Strategies

Early referral for appropriate developmental and educational services is vital for HHS and should take place within the first few months of life. Children with combined vision and hearing loss may be classified as "deaf-blind," even when residual hearing and vision is present. As such, they are eligible to receive specialized services from educational consultants trained to deal with dual sensory impairment. An early childhood educator who has expertise with dual sensory impairment may not be locally available, but can usually be accessed at the regional or state level. Before entry into the school system, these children should receive a preschool assessment by an expert in deaf-blindness. Children with HHS often show significant early delays, but may excel once they develop mobility and an effective communicative system [Davenport et al., 1986; Blake and Brown, 1993].

The assessment and educational placement of children with multi-sensory impairment is complex, with far-reaching implications [McInnes and Treffry, 1982; Best, 1983; Fox, 1983; Bond, 1986; Goldson et al., 1986; Blake and Brown, 1993]. There are a number of children with HHS who present with severe multi-sensory impairment and profound developmental delay in the early years, who ultimately function well in mainstreamed educational settings with only minimal additional support. Many parents, who initially received a prediction of profound mental retardation, have noted improvements in their child's capabilities, once they were placed in an appropriate educational setting and developed a functional communication system. Parents often find themselves acting as primary coordinators for educational services, and they benefit from interactions with appropriate parent support groups. Such groups offer a rich resource of written information, as well as local and regional advocacy expertise from other parents and service providers, and they help to put parents in touch with other parents of children with the same condition.

In light of these observations, the best educational program for children with HHS will include language-based communication goals utilizing total communication (signs, gestures, objects, pictures, and printed as well as spoken words).

Maladaptive Behavioral Intervention Strategies

The following intervention strategies may help to lessen some maladaptive behaviors commonly present in individuals with HHS. These children need to be taught how to make choices, how to help out, how to be social, how to be part of a group, how to negotiate, how to be organized, and how to anticipate activities (preferably through a graduated calendar system). Their curriculum should be highly organized with structured content that teaches functional skills as well as early developmental concepts. Other studies in this series provide specific recommendations. There must be repetition of language, with vocabulary building through active participation in social activities and experiential learning within a natural environment that teaches the child to reduce the high stress levels associated with trying to learn through markedly reduced sensory inputs [Brown, 2004]. In some children with HHS, behavioral management and/or judicious use of medications may also be indicated [van Dijk and de Kort, 2004; Williams et al., 2004]. In all children with HHS, an effective educational plan that recognizes the impact of dual sensory impairment will result in the most successful outcomes.

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