

## Psychiatric Diagnoses and Psychotropic Medications in CHARGE Syndrome: A Pediatric Survey

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**Abstract** Many children diagnosed with CHARGE syndrome demonstrate behavioral difficulties in addition to visual, hearing and other systemic impairments. Previous research has reported that children with CHARGE have increased rates of self-injury and aggression, as well as increased frequency of obsessive compulsive and autism spectrum disorders. This study asked parents to report not only the diagnoses given for their child's behavior problems, but also whether psychotropic medication interventions were prescribed, and which agents were chosen. Results of this study showed that according to parental report, anxiety disorders and pervasive developmental disorders were the most common psychiatric diagnoses assigned with antidepressant and antipsychotic medications the most frequently prescribed psychopharmacological agents.

**Keywords** CHARGE syndrome · Deafblindness · Autism · Anxiety · Psychotropics

CHARGE syndrome is a genetic disorder of multiple congenital abnormalities originally described in 1979 by two separate clinicians (Hall 1979; Hittner *et al.* 1979). CHARGE is one of the most common causes of deafblindness, with prevalence of CHARGE ranging from 1/10,000 to 1/15,000 live births. (Issekutz

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*et al.* 2005; Stromland *et al.* 2003) The acronym was suggested by Pagon and colleagues (1981), and represents Coloboma, Heart defects, Atresia choanae, Retarded growth and development, Genital hypoplasia and Ear abnormalities. Since that time, various clinical diagnostic criteria have been developed based on clusters of major and minor criteria, with the major criteria including (1) colobomas of the iris, retina, choroid or optic disk, (2) choanal atresia or stenosis, (3) ear anomalies of the inner, middle or external ear and (4) cranial nerve abnormalities (Blake *et al.* 1998; Oley *et al.* 1988; Tellier *et al.* 1998; Verloes 2005). There have also been significant advances in the understanding of the genetics of CHARGE, with the discovery of a microdeletion of chromosome 8q12.1 in individuals with CHARGE, and detection of mutations in the CHD7 gene in this region. The CHD7 gene is known to encode a protein from the chromodomain family, which plays a crucial role in early embryonic development (Jongmans *et al.* 2005; Lalani *et al.* 2006; Vissers and van Ravenswaaij 2004). Indeed, the various congenital anomalies seen in CHARGE are believed to originate from abnormalities of the embryonic neural crest (Tellier *et al.* 1998; Verloes 2005).

Due to the potential for significant systemic dysfunction, survival is the most prominent goal in the first years of life (Souriau *et al.* 2005). But for many surviving children with CHARGE, behavior disorders subsequently become central health issues (Blake *et al.* 1998; Issekutz *et al.* 2005; Tellier *et al.* 1998). Problem behaviors, such as self-injury and aggression, and additional psychopathology in CHARGE have also been the subject of much interest and research in the recent years, although they do not constitute additional criteria for the CHARGE diagnosis.

It is not surprising that individuals with CHARGE have a propensity towards behavioral and psychiatric disturbance. Multiple well-known genetic syndromes have behavioral and psychiatric difficulties as part of their proposed behavioral phenotype, including, but certainly not limited to, Cornelia de Lange, Fragile X, Lesch-Nyhan, Prader-Willi, Smith–Lemli–Opitz and Smith–Magenis syndromes (Berney *et al.* 1999; Harris 1998; Schroeder *et al.* 2001; Tierney *et al.* 2001; Willekens *et al.* 2000). While not all children with CHARGE syndrome have intellectual disability (ID), many do experience developmental delay with adaptive dysfunction (Salem-Hartshorne and Jacob 2005). This is salient in that there is an increased prevalence of both problematic behaviors and psychiatric illness in those with intellectual disability compared to the general population (Borthwick-Duffy 1994; Colucci *et al.* 1998, Jacobson 1982; MacLean 1993, Matson and Sevin 1994; White *et al.* 2005). In fact, the mere presence of problem behaviors in ID carries up to a threefold risk of psychiatric illness (Rojahn *et al.* 2004).

In addition to the roles of genetics and ID in the potential development of behavioral and psychiatric pathology, children with CHARGE may be further prone to such due to their vision and hearing deficits. Sensory impairments can negatively impact on social and interpersonal interactions (Eaton and Menolascino 1982), and combined visual and hearing impairments may have negative effects on behavior, “resulting in more restricted adaptive behavior and problem-solving repertoires” (Matson and Sevin 1994). The American Academy of Mental Retardation lists sensory deficit as an additional “stressor” that may lead to behavioral disturbance (AAMR 2000). Self-injury and aggression have been reported as commonly seen in

the blind and deaf-blind of various etiologies (Carvill 2001), and Van Dijk recently emphasized parental report of behavioral disturbance from colobomata-related visual disturbance in CHARGE (Van Dijk and de Kort 2005).

Studies of behavioral disturbance in CHARGE have revealed a significant level of problem behaviors in general. Souriau *et al.* reported a prevalence of 40% for self-injury and 38% for aggression in 71 people with CHARGE (Souriau *et al.* 2005). Van Dijk and de Kort found that 54% of individuals with CHARGE engaged in self-injury (Van Dijk and de Kort 2005) while Thelin and Fussner reported rates of 61% for self-stimulatory behavior, 46% for aggression, and 32% for unstable or explosive behavior (Thelin and Fussner 2005).

Additional research into actual psychiatric diagnosis in CHARGE has also been informative, with much evidence pointing towards the existence in CHARGE of both obsessive-compulsive disorder and autistic features. (Bernstein and Denno 2005; Hartshorne and Cypher 2004; Hartshorne *et al.* 2005; Smith *et al.* 2005a, b). Multiple studies have shown frank autistic-like behaviors in CHARGE, although the CHARGE profile differs from that of autistic children without dual sensory impairment and autistic children with dual sensory impairment of another etiology (Fernell *et al.* 1999; Hartshorne and Cypher 2004; Smith *et al.* 2005b). Many individuals raising, educating or treating children with CHARGE also feel that obsessive compulsive disorder (OCD) may indeed be part of the syndrome. One CHARGE parent described the obsessive behaviors of her son “as if his mind got stuck in a rut,” including sorting, lining and checking behaviors (Bernstein and Denno 2005; Lauger *et al.* 2005). Souriau has also reported anxiety and depression in CHARGE, with rates of 31 and 24%, respectively, in a 71 patient French study (Souriau *et al.* 2005).

During their work in the CHARGE community, the authors have become well aware of the large number of children with CHARGE currently being assessed by mental health professionals, given psychiatric diagnoses and prescribed psychotropic, or “behavioral,” medications, particularly to target the specific behavioral and psychiatric disturbances reviewed above as common in CHARGE. This raises many important questions surrounding psychiatric diagnoses given and psychotropic medications subsequently chosen for children and adults with CHARGE. We would like to know more about single or multiple psychiatric diagnoses being given in CHARGE, and the presenting concerns that led to these diagnoses. We would also like to discover which classes of medications are being selected to target specific psychiatric symptoms or diagnoses in CHARGE, and whether individuals are being treated with single agents or polypharmacy. Although not a component of this study, we are also eager to ultimately assess the efficacy of particular psychotropic medications in behavioral disturbance of CHARGE, as well as learn of any CHARGE-specific side effects of psychotropics and potential pitfalls of CHARGE psychopharmacology. We are hopeful that in the future this preliminary study can be further developed to delve into relationships between psychiatric diagnoses, psychotropics and other important components of CHARGE, including sensory deficits, communicative competence, mobility, underlying somatic illness and adaptive function. In the meantime, our early discoveries will guide us in improving assessment and treatment for the many individuals with CHARGE currently impaired by myriad behavioral and psychiatric concerns.

## Materials and Methods

### Participants

Materials were mailed to parents of 102 children aged 6–18 who had participated in previous research conducted by the second author. All of these families had participated in at least two previous studies, and in some cases four, and were considered to be reliable informants. Materials were returned by 89 of the parents, for an 87% return rate. Two sets of materials were not usable, and thus analyses are based on 87 children.

### Materials

#### *CHARGE History Questionnaire*

This 16 item form, based on one developed by Salem-Hartshorne and Jacob (2004), gathered information on basic demographics, the child's CHARGE features, age of walking, and information on vision and hearing. They were also specifically asked to "please indicate any diagnoses given to your child for her/his behavior (such as autism)," and "what medications and herbal supplements is your child taking on a regular basis?"

#### *Developmental Behaviour Checklist, second edition (DBC, Dekker et al. 2002)*

The DBC was developed to measure the behavioral problems of children and adults with cognitive disabilities. It can be completed by the parent. There are 96 items scored in five subscales (disruptive/antisocial, self-absorbed, communication disturbance, anxiety, social relating). The scales were derived through factor analysis (Einfeld and Tonge 1995), and confirmed by Hastings *et al.* (2001) who also replicated high levels of internal consistency. The DBC has been demonstrated to be a valid measure of change in young people with cognitive disabilities (Clarke *et al.* 2003).

## Results

Of the 87 usable questionnaires, 78 (89.7%) were completed by the mother. A majority of the children were male (59.3%), and they came from 27 states, the largest number (9) from New Jersey. They were predominantly Caucasian (88.5%), with three Hispanic, one Asian/Pacific Islander, and six of unknown racial/ethnic background. Ages ranged from 6–18, with a mean of 11.1 (SD=3.66). The percentage of children with the various CHARGE characteristics is shown in Table 1.

### Diagnoses

Parents were asked to list any diagnoses given to their child "for their behavior." This question was open-ended, without request for details such as age when diagnoses were given, or source(s) of diagnosis, such as pediatrician, neurologist, psychiatrist, psychologist or other. Thirty-four (39%) listed at least one diagnosis. However, some of the diagnoses were not specifically psychiatric and were eliminated, such as

**Table 1** Medical problems in the sample

Condition	Percent (N=87)
Delayed motor milestones	99
Vestibular problems	85
Sensorineural hearing loss	85
Coloboma	84
Characteristic CHARGE ear	83
Growth deficiency	82
Frequent middle ear infections	79
Heart defect	78
Swallowing problems	70
Genital hypoplasia	62
Choanal atresia or stenosis	60
Facial palsy	48
Anosmia	40
Spine anomalies	31
Renal problems	30
Cleft lip or palate	29
Tracheosophageal fistula	22
Hand anomalies	17
Abdominal defects	14
Thymic/parathyroid hypoplasia	6

“behavior problems” and “deafblind.” This left 32 participants (37%) with at least one identified behavioral diagnosis. The number of diagnoses ranged from 1 to 5, with an average of 1.78 diagnoses ( $SD=1.07$ ). These diagnoses were categorized, and are presented in Table 2. The largest category was anxiety disorders with 17 children so diagnosed. Two of these were diagnosed with both anxiety disorder and OCD, and one had both of these diagnoses in addition to “Perseverations.” The second largest

**Table 2** Psychiatric diagnoses

Diagnosis	N
ADHD	11
Anxiety disorders	17
Anxiety	5
OCD	15
Perservations	1
Pervasive developmental disorders	14
Autism	8
Asperger's	2
PDD	6
Disruptive behavior disorders	2
ODD	1
Rage behavior	1
Stereotypic movement disorders	1
Self injurious behavior	1
Mood disorders	3
Mood disorder	1
Depression	1
Bipolar	1
Psychotic disorders	1
Hallucinations	1

**Table 3** Comorbidity of psychiatric diagnoses

	OCD	ADHD	Autism	PDD	Anxiety	Other
OCD	6	3	2	2	3	4 <sup>a</sup>
ADHD		3	4	2	1	2 <sup>b</sup>
Autism			4	1	0	2 <sup>b</sup>
PDD				2	0	2 <sup>c</sup>
Anxiety					1	3 <sup>d</sup>
Other						2 <sup>c</sup>

<sup>a</sup> Perseverations, hallucinations, mood disorder, bipolar

<sup>b</sup> Aspergers, ODD

<sup>c</sup> Aspergers, ODD, bipolar

<sup>d</sup> Perseverations, hallucinations, mood disorder

<sup>e</sup> SIB's and Aspergers each appeared by itself once

group was Pervasive Developmental Disorder (PDD) with 14 children. Interestingly, one child was diagnosed with Autism, Aspergers's, and PDD, although it was not known whether these diagnoses were given concomitantly, or at different times by different providers. Eleven children had an ADHD diagnosis. Children also had multiple diagnoses across categories. Eighteen had only one diagnosis, six had two, and another six had three, while one had four and one more had five. The five diagnoses of the last child were Autism, Asperger's, PDD, ADHD and ODD, and thus three fell into the same diagnostic classification. Table 3 shows the number of times a particular diagnosis was associated with others. It also shows in the diagonal, the number of times each diagnosis appeared by itself. OCD was the most frequent diagnosis to appear by itself, followed by autism and then ADHD.

In order to learn whether having a diagnosis was related to the severity of the child's behavior, the 32 children with a diagnosis were compared to the 55 without on the Developmental Behavior Checklist. Means for the two groups as well as *t*-tests of the significance of the difference between the means on the total DBC scores and for each of the subscales are reported in Table 4. As can be seen, differences were significant in each case. Those who had a behavioral diagnosis had higher, or more severe, scores on the DBC and each subscale. In order to learn more

**Table 4** Developmental Behavior Checklist scores for those with and without psychiatric diagnoses

Scale	Diagnosis		No Diagnosis		<i>t</i> -test (df)
	<i>N</i>	Mean (SD)	<i>N</i>	Mean (SD)	
Total score	32	58.34 (21.78)	55	35.85 (21.03)	4.75 (85)***
Disruptive	32	15.34 (7.51)	55	8.16 (6.35)	4.75 (85)***
Self absorbed	32	21.13 (10.43)	55	14.05 (10.52)	3.03 (85)**
Communication	32	8.88 (3.84)	55	5.16 (4.22)	4.08 (85)***
Anxiety	32	4.78 (3.46)	55	3.29 (2.53)	2.31 (85)*
Social	32	6.34 (3.53)	55	3.84 (3.68)	3.11 (85)**

\* $p < 0.05$

\*\* $p < 0.01$

\*\*\* $p < 0.001$

about how the subscales of the DBC might predict whether a child received a diagnosis, logistic regression was applied. Each of the subscales of the DBC was entered stepwise into the logistic equation for having a diagnosis. Only the Disruptive subtest met the criteria for entry and provided a significant model chi square ( $1, N=87$ )=19.09,  $p=0.000$ . A Nagelkerke R Square was 0.27, indicating that about 27% of the variance is accounted for. Ability to correctly predict whether or not the child had a diagnosis improved from 63.2 to 71.3.

## Medications

Parents were asked to list medications their child was taking on a regular basis. Thirty-seven (43%) were on at least one psychotropic. Fifteen were on one, 13 were on two, eight were on three, and one person was on five psychotropics, including dextroamphetamine, haloperidol, risperidone, lorazepam, and clonidine (a stimulant,

**Table 5** Psychotropic medications

Medication	<i>N</i>
Stimulants	8 (6 on one stimulant, 2 on two)
Dextroamphetamine	3
Methylphenidate	4
Atomoxetine	2
“ADHD meds”	1
Antipsychotics	11 (11 on one, 1 on two)
Aripiprazole	3
Haloperidol	1
Risperidone	6
Quetiapine	1
Olanzapine	1
Anxiolytics	3
Lorazepam	1
Clonazepam	1
Alprazolam	1
Antidepressants	21 (20 on one, 1 on two)
Clomipramine	2
Citalopram	3
Amitriptyline	1
Escitalopram	2
Fluvoxamine	4
Paroxetine	2
Fluoxetine	5
Bupropion	1
Sertraline	2
Mood stabilizers	6 (3 on one, 3 on two)
Valproic acid	4
Felbamate	1
Levetiracetam	1
Gabapentin	1
Topiramate	2
Antinarcotics	1
Modafinil	1
Antihypertensives	12
Clonidine	11
Propranolol	1

two antipsychotics, an anxiolytic and an antihypertensive). Medications and their frequency are categorized in Table 5. Most frequently prescribed individual drug was clonidine at 11, followed by risperidone at six and fluoxetine at five. The largest category of drugs was antidepressants, particularly the selective serotonin reuptake inhibitors (SSRIs), fluoxetine, fluvoxamine, and citalopram. The second largest category was antihypertensives due to the high number of children on the alpha-agonist clonidine. Although only one child was indicated to have a diagnosis of actual psychosis, antipsychotics were the third largest category of drugs. In addition to 11 children prescribed risperidone, three children were on aripiprazole. Stimulants were the next largest group, followed by mood stabilizers.

### Medications by Diagnosis

Medications by diagnosis are shown in Table 6. In interpreting this table, it is important to keep in mind that many children had multiple diagnoses. There is an added category of “none listed” as 13 children with no psychiatric diagnosis noted by their parents were nevertheless on medications. The largest number of medications was used for ADHD and anxiety diagnoses. For ADHD the largest category was antihypertensives, followed by stimulants and then antipsychotics. For anxiety the medication category most frequently chosen was antidepressants, followed by antipsychotics.

### Predicting Medication Use

As the absolute number of medications the child is on may be indicative of the overall severity of the behavior, it was of interest to look for any correlations with the DBC, as well as with age, and with age of walking. Age of walking has been found in other studies to be a marker for behavioral, cognitive, and communication difficulties (Hartshorne and Cypher 2004, Hartshorne *et al.* 2005, Salem-Hartshorne and Jacob 2004, 2005, Thelin and Fussner 2005). In this sample, the average age walked with nearly 3 years 3 months, with the range from 1 year 3 months to 8 years 6 months.

In the initial analysis, only those children who were on at least one medication were included, a sample size of 27. Results are reported in Table 7. Total score on the DBC was not significantly correlated; however the subscales of Self-absorbed

**Table 6** Psychotropics by diagnosis

Diagnosis	Anti-hypertensives	Stimulants	Anti-psychotics	Anxiolytics	Anti-depressants	Mood stabilizers	Anti-narcoleptic
ADHD	8	5	3	1	2		
Psychotic			1		1		
Stereotypic	1				1		
Disruptive	1		2		2		
Mood	1		1		3	1	
Anxiety	3	1	6	2	10	2	1
PDD	4	3	5		6		
None Indicated	5	3	2	1	5	4	

**Table 7** Correlations with number of medications

	Age	Walk	DBC	Disrupt	Absorb	Comm	Anxiety	Social
Number of meds	0.17	0.51**	0.22	0.08	0.35*	-0.06	-0.10	0.45**

\* $p < 0.05$ \*\* $p < 0.01$ 

and Social were significantly correlated. Chronological age was not significantly correlated; however, age of walking was, such that the older the child walked the more medications the child was taking.

Another way to answer this question is to compare those children who were on at least one medication with those who were on none. Independent *t*-tests were conducted using age, age of walking, and the DBC total and subscale scores. The only significant difference was found for the DBC scale of Disruptive ( $t=2.35$ ,  $df=85$ ,  $p < 0.05$ ). Those children who were taking at least on medication had higher scores on the disruptive scale than those who were not taking medications.

## Discussion

This pilot study reveals important information on psychiatric diagnosis and psychotropic medication usage in individuals with CHARGE, despite its limitation as being based on parental report, which limits the certainty of diagnosis given and accuracy of such, as well as rationale for drug use and ultimate therapeutic efficacy. However, this study demonstrates that various psychiatric diagnoses as a whole are frequently assigned to children with CHARGE. It also lends support for previous reports of high frequencies of OCD, PDD, and ADHD diagnoses in the CHARGE population (Hartshorne and Cypher 2004).

In this sample of children with CHARGE, we further discovered that multiple medication classes are being utilized, with antidepressants the most frequently chosen category of agents, the most common being selective serotonin reuptake inhibitors. The second largest category of agents prescribed was antihypertensives, and clonidine was actually the most frequently prescribed *individual* agent in the study. Antipsychotics constituted the third most likely prescribed class of medications in this patient sample.

Because the age at which the child first walks has been found to be a marker of how well the child with CHARGE develops, it was of interest to see whether the use of medication was related. Indeed, looking only at those children who were on at least one medication, the more medications they were on was associated with the age they first walked, so that late walkers were more likely to be on more medications than early walkers. While age of walking is an indicator of possible developmental difficulties (behavior, cognition, communication), and was found here to be related to how many medications a child may be taking, it did not help to differentiate whether or not children were on any medication. Chronological age, in distinction to age of walking, was not related to medication use. Total scores on the DBC were

also not related; however, some of the subscales of the DBC were, suggesting that behavior is related to medication usage, but not as strongly as it was related to having a diagnosis.

In comparing medication classes with diagnostic classes, we learned that ten of the patients prescribed antidepressants were diagnosed with an anxiety disorder, with the most common anxiety disorder being obsessive-compulsive disorder. Again, this study does not provide us with information regarding the validity of the diagnoses given, nor rationale for medication selection. However, reported usage of antidepressants for anxiety disorders in CHARGE is intriguing since these medications, especially SSRIs, have a proven track record in ameliorating anxiety and obsessive and compulsive symptoms, (Fineberg and Gale 2005; Geller *et al.* 2003; Lewin *et al.* 2005), and have also been studied in intellectual disability with positive results and few side effects (Buitelaar and Willemsen-Swinkels 2000; Janowsky *et al.* 2005). Indeed, usage of SSRIs in CHARGE for potential anxiety appears to be a very promising angle for treatment and future research. The authors have personally had much positive experience with SSRIs usage in children with CHARGE, particularly at low dosages. At the 2005 CHARGE conference in Miami, one adult participant personally related her positive experience with SSRIs and felt that such had allowed her to experience significant relief from symptoms of OCD.

Our study also suggests that children with CHARGE may be prescribed antihypertensives and stimulants for given diagnoses of ADHD, as well as SSRIs and antipsychotics for diagnoses of PDD.

Because challenging behavior has become so frequently associated with CHARGE, we were also interested to see whether those children who had a psychiatric diagnosis were actually more significantly behavioral disordered than those without. The differences proved to be highly significant on the Developmental Behavior Checklist. Those children with the most challenging behavior were the ones who received the diagnoses.

## Conclusion

Behavioral and psychiatric disturbance are frequently found in individuals with CHARGE syndrome. This study is the first of its kind to assess both psychiatric diagnoses and medications given for behavioral concerns in CHARGE. Based on parental report, our results suggest increased rates of anxiety disorders and pervasive developmental disorders in CHARGE, and also reveal that some children with CHARGE carry multiple psychiatric diagnoses. Our data on psychotropic medication usage in CHARGE shows that psychoactive medications are frequently prescribed, with antidepressants, especially SSRIs, being the most commonly prescribed agents, followed by antihypertensives and antipsychotics. Success of these agents in CHARGE is currently unknown.

Further research in the CHARGE population is needed to evaluate actual diagnostic accuracy, rationale for use of various psychotropics, and efficacy of medication treatment based on standardized measures or clinician report. Such research would also need to consider that while classic usage of the DSM-IV-TR

criteria is generally thought accurate and appropriate for those with mild to moderate mental retardation, such may not be true for the more severely cognitive impaired. (MacLean 1993; AAMR 2000).

It is also imperative to recognize that psychotropic intervention need not be the only therapeutic venue for children with CHARGE and psychiatric disturbance. Decades of research support the successful usage of applied behavioral analysis in the resolution of psychiatric pathology in individuals with developmental disabilities (Kahng *et al.* 2002; Herbert *et al.* 2002; Matson *et al.* 1996). In addition, sensory integration techniques, widely used by occupational therapists (Schaaf and Miller 2005), are demonstrating some success with autism (Iarocci and McDonald 2006) and with self-stimulatory and self-injurious behaviors (Smith *et al.* 2005a), and have been recommended for CHARGE (Brown 2005). Additionally, it is known that psychotropic medications are frequently overused in the developmentally disabled population, at times without specific diagnosis and for overall suppression of negative behaviors via sedation (Baumeister and Sevin 1989; Friedlander *et al.* 2001, LaMalfa *et al.* 2006; Matson *et al.* 2000). A wide net should be cast for effective treatment interventions in psychiatric disturbance in CHARGE.

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## References

- American Association of Mental Retardation (2000). Treatment of psychiatric and behavioral problems in mental retardation. *American Journal of Mental Retardation*, 105(3), 165–188.
- Baumeister, A. A., & Sevin, J. A. (1989). Pharmacological control of aberrant behavior in the mentally retarded: Toward a more rational approach. *Neuroscience & Biobehavioral Reviews*, 14, 253–262.
- Berney, T. P., Ireland, M., & Burn, J. (1999) Behavioral phenotype of Cornelia de Lange syndrome. *Archives of Disease in Childhood*, 81, 333–336.
- Bernstein, V., & Denno, L. S. (2005). Repetitive behaviors in CHARGE syndrome: Differential diagnosis and treatment options. *American Journal of Medical Genetics*, 133A, 232–239.
- Blake, K. D., Davenport, S. L. H., Hall, B. D., Hefner, M. A., Pagon, R. A., Williams, M. S., *et al.* (1998). CHARGE association: An update and review for the primary pediatrician. *Clinical Pediatrics*, 37, 159–174.
- Borthwick-Duffy, S. A. (1994). Epidemiology and prevalence of psychopathology in people with mental retardation. *Journal of Consulting and Clinical Psychology*, 62(1), 17–27.
- Brown, D. (2005). CHARGE syndrome “behaviors:” Challenges or adaptations? *American Journal of Medical Genetics*, 133A, 268–272.
- Buitelaar, J. K., & Willemsen-Swinkels, S. H. N. (2000). Medication treatment in subjects with autistic spectrum disorders. *European Child and Adolescent Psychiatry*, 9(1), 85–97.
- Carvill, S. (2001). Sensory impairments, intellectual disability and psychiatry. *Journal of Intellectual Disability Research*, 45(6), 467–483.
- Clarke, A. R., Tonge, B. J., Einfeld, S. L., & Mackinnon, A. (2003). Assessment of change with the Developmental Behaviour Checklist. *Journal of Intellectual Disabilities Research*, 47(Pt 3), 210–212.
- Colucci, G., Pellicciotta, A., Buono, S., & Di Nuovo, S. F. (1998). The Rorschach Egocentricity Index in subjects with intellectual disability: A study on the incidence of different psychological pathologies. *Journal of Intellectual Disability Research*, 42(5), 354–359.
- Dekker, M. C., Nunn, R. J., Einfeld, S. E., Tonge, B. J., & Koot, H. M. (2002). Assessing emotional and behavioral problems in children with intellectual disability: Revisiting the factor structure of the developmental behavior checklist. *Journal of Autism and Developmental Disorders*, 32(6), 601–610.
- Eaton, L. F., & Menolascino, F. J. (1982). Psychiatric disorders in the mentally retarded: Types, problems and challenges. *American Journal of Psychiatry*, 139(10), 1297–1303.

- Einfeld, S. L., & Tonge, B. J. (1995). The Developmental Behavioral Checklist: The development and validation of an instrument to assess behavioral and emotional disturbance in children and adolescents with mental retardation. *Journal of Autism and Developmental Disorders*, 25(2), 81–104.
- Fernell, E., Olsson, V. A., Karlgren-Leitner, C., Norlin, B., Hagberg, B., & Gillberg, C. (1999). Autistic disorders in children with CHARGE association. *Developmental Medicine and Child Neurology*, 41(4), 270–272.
- Fineberg, N. A., & Gale, T. M. (2005). Evidence-Based pharmacotherapy of obsessive-compulsive disorder. *International Journal of Neuropsychopharmacology*, 8, 107–129.
- Friedlander, R., Lazar, S., & Klancnik, J. (2001). Atypical antipsychotic use in treating adolescents and young adults with developmental disabilities. *Canadian Journal of Psychiatry*, 46(8), 741–745.
- Geller, D. A., Biederman, J., Stewart, S. E., Mullin, B., Martin, A., Spencer, T., et al. (2003). Which SSRI? A meta-analysis of pharmacotherapy trials in pediatric obsessive-compulsive disorder. *American Journal of Psychiatry*, 160, 1919–1928.
- Hall, B. D. (1979). Choanal atresia and associated multiple anomalies. *Journal of Pediatrics*, 95(3), 395–398.
- Harris, J. C. (1998). *Developmental neuropsychiatry volume II: Assessment, diagnosis and treatment of developmental disorders*. New York: Oxford University Press.
- Hartshorne, T. S., & Cypher, A. D. (2004). Challenging behavior in CHARGE syndrome. *Mental Health Aspects of Developmental Disabilities*, 7(2), 41–52.
- Hartshorne, T. S., Grialou, T. L., & Parker, K. R. (2005). Autistic-like behavior in CHARGE syndrome. *American Journal of Medical Genetics*, 133A, 257–261.
- Hastings, R. P., Brown, T., Mount, R. H., & Cormack, K. F. (2001). Exploration of psychometric properties of the developmental behavior checklist. *Journal of Autism and Developmental Disorders*, 31(4), 423–431.
- Herbert, J. D., Sharp, I. R., & Gaudiano, B. A. (2002). Separating fact from fiction in the etiology and treatment of autism: A scientific review of the evidence. *Scientific Review of Mental Health Practice*, 1, 23–43.
- Hittner, H. M., Hirsch, N. J., Kreh, G. M., & Rudolph, A. J. (1979). Colobomatous microphthalmia, heart disease, hearing loss, and mental retardation—A syndrome. *Journal of Pediatric Ophthalmology and Strabismus*, 16(2), 122–127.
- Iarocci, G., & McDonald J. (2006). Sensory integration and the perceptual experience of persons with autism. *Journal of Autism and Developmental Disabilities*, 36, 77–90.
- Issekutz, K. A., Graham, J. M., Prasad, C., Smith, I. M., & Blake, K. D. (2005). An epidemiological analysis of CHARGE syndrome: Preliminary results from a Canadian study. *American Journal of Medical Genetics*, 133A, 309–317.
- Jacobson, J. W. (1982). Problem behavior and psychiatric impairment within a developmentally disabled population I: Behavior frequency. *Applied Research in Mental Retardation*, 3, 121–139.
- Janowsky, D. S., Shetty, M., Barnhill, J., Elamir, B., & Davis, J. M. (2005). Serotonergic antidepressant effects on aggressive, self-injurious and destructive/disruptive behaviors in intellectually disabled adults: A retrospective, open-label, naturalistic trial. *International Journal of Neuropsychopharmacology*, 8, 37–48.
- Jongmans, M. C. J., Admiraal, R. J., van der Donk, K. P., Vissers, E. L. M., Baas, A. F., Kapusta, L., et al. (2005). CHARGE syndrome: The phenotypic spectrum of mutations in the CHD7 gene. *Journal of Medical Genetics*, 43(4), 306–314.
- Kahng, S., Iwata, B. A., & Lewin, A. (2002). Behavioral treatment of self-injury, 1964–2000. *American Journal of Mental Retardation*, 107, 212–221.
- Lalani, S. R., Safiullah, A. M., Fernbach, S. D., Harutyunyan, K. G., Thaller C., Peterson, L. E., et al. (2006). Spectrum on CHD7 mutations in 110 individuals with CHARGE syndrome and genotype-phenotype correlation. *The American Journal of Human Genetics*, 78, 303–314.
- LaMalfa, G., Lassi, S., Bertelli, M., & Castellani, A. (2006). Reviewing the use of psychotropic drugs in people with intellectual disability. *Human Psychopharmacology*, 21, 73–89.
- Lauger, K., Cornelius, N., & Keedy, W. (2005). Behavioral features of CHARGE syndrome: Parents' perspectives of three children with CHARGE syndrome. *American Journal of Medical Genetics*, 133A, 291–299.
- Lewin, A. B., Storch, E. A., Adkins, J., Murphy, T. K., & Geffken, G. R. (2005). Current directions in pediatric obsessive-compulsive disorder. *Pediatric Annals*, 34(2), 128–134.
- MacLean, W. E. (1993). Overview. In J. L. Matson, & R. P. Barrett (Eds.), *Psychopathology of the mentally retarded* (2nd edn.) (pp. 1–16). Simon & Schuster.
- Matson, J. L., Bamburg, J. W., Mayville, E. A., Pinkston, J., Bielecki, J., Kuhn, D. E., et al. (2000). Psychopharmacology and mental retardation: A 10 year review (1990–1999). *Research in Developmental Disabilities*, 21, 263–296.

- Matson, J. L., Benavidiz, D., Compton, L., Paclawskyj, & T. R., Baglio, C. (1996). Behavioral treatment of autistic persons: A review of research from 1980 to present. *Research in Developmental Disabilities, 17*, 433–465.
- Matson, J. L., & Sevin, J. A. (1994). Theories of dual diagnosis in mental retardation. *Journal of Consulting and Clinical Psychology, 62*(1), 6–16.
- Oley, C. A., Baraitser, M., & Grant, D. B. (1988). A reappraisal of the CHARGE association. *Journal of Medical Genetics, 25*(3), 147–156.
- Pagon, R. A., Graham, J. M., Zonana, J., & Yong, S. L. (1981). Coloboma, congenital heart disease, and choanal atresia with multiple anomalies: CHARGE association. *Journal of Pediatrics, 99*(2), 223–227.
- Rojahn, J., Matson, J. L., Naglieri, J. A., & Mayville, E. (2004). Relationships between psychiatric conditions and behavior problems among adults with mental retardation. *American Journal on Mental Retardation, 109*(1), 21–33.
- Salem-Hartshorne, N., & Jacob, S. (2004). Characteristics and development of children with CHARGE association/syndrome. *Journal of Early Intervention, 26*, 292–301.
- Salem-Hartshorne, N., & Jacob, S. (2005). Adaptive behavior in children with CHARGE syndrome. *American Journal of Medical Genetics, 133A*, 262–267.
- Schaaf, R. C., & Miller, L. J. (2005). Occupational therapy using a sensory integrative approach for children with developmental disabilities. *Mental Retardation and Developmental Disabilities Research Reviews, 11*, 143–148.
- Schroeder, S. R., Oster-Granite, M. L., Berkson, G., Bodfish, J. W., Breese, G. R., Cataldo, M. F., et al. (2001). Self-injurious behavior: Gene–brain–behavior relationships. *Mental Retardation and Developmental Disabilities Research Reviews, 7*, 3–12.
- Smith, S. A., Koenig, K. P., & Kinnealy, M. (2005a). Effects of sensory integration intervention on self-stimulating and self-injurious behaviors. *American Journal of Occupational Therapy, 59*, 418–425.
- Smith, I. M., Nichols, S. L., Issekutz, I., & Blake, K. D. (2005b). Behavioral profiles and symptoms of autism in CHARGE syndrome: Preliminary Canadian Epidemiological Data. *American Journal of Medical Genetics, 133A*, 248–256.
- Stromland K., Miller, M., Ekman-Joelsson, B. M., Sjogreen, L., Andersson-Norinder, J., Jacobsson C., et al. (2003). Malformations in CHARGE association arise during a limited time period early in pregnancy. *Birth Defects Research, 67*, 316.
- Souriau, J., Gimenes, M., Blouin, C., Benbrik, I., Benbrik, E., Churakowskyi, A., et al. (2005). CHARGE syndrome: Developmental and behavioral data. *American Journal of Medical Genetics, 133A*, 278–281.
- Tellier, A. L., Cormier-Daire, V., Abadie, V., Amiel, J., Sigaudy, S., Bonnet D., et al. (1998). CHARGE Syndrome: Report of 47 Cases and Review. *American Journal of Medical Genetics, 76*, 402–409.
- Theelin, J. W., & Fussner, J. C. (2005). Factors related to the development of communication in CHARGE syndrome. *American Journal of Medical Genetics, 133A*, 282–290.
- Tierney, E., Nwokoro, N. A., Porter, F. D., Freund, L. S., Ghuman, J. K., & Kelley, R. I. (2001). Behavioral phenotype in the RSH/Smith–Lemli–Opitz syndrome. *American Journal of Medical Genetics, 98*, 191–200.
- Van Dijk, J. P. M., & de Kort, A. (2005). Reducing challenging behaviors and fostering efficient learning of children with CHARGE syndrome. *American Journal of Medical Genetics, 133A*, 273–277.
- Verloes, A. (2005). Updated diagnostic criteria for CHARGE syndrome: A proposal. *American Journal of Medical Genetics, 133A*, 306–308.
- Vissers, L. E. L. M., & van Ravenswaaij, C. M. A. (2004). Mutations in a new member of the chromodomain gene family cause CHARGE syndrome. *Nature Genetics, 36*(9), 955–957.
- White, P., Chant, D., Edwards N., Townsend, C., Waghorn, G. (2005). Prevalence of intellectual disability and comorbid mental illness in an Australian community sample. *Australian and New Zealand Journal of Psychiatry, 39*, 395–400.
- Willekens, D., DeCock, P., & Fryns, J. P. (2000). Three young children with Smith–Magenis syndrome: Their distinct, recognizable behavioural phenotype as the most important clinical symptoms. *Genetic Counseling, 11*(2), 103–110.