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Autism Spectrum Disorders and Symptoms in Children with Molecularly Confirmed 22q11.2 Deletion Syndrome

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Abstract

In this study, we assessed the presence of autism spectrum disorders (ASD) among children with a confirmed 22q11.2 deletion (n = 98). The children's caregivers completed screening measures of ASD behaviors, and for those whose scores indicated significant levels of these behaviors, a standardized diagnostic interview (Autism Diagnostic Interview-Revised; ADI-R) was administered. Results demonstrated that over 20% of children (n = 22) were exhibiting significant levels of autism spectrum symptoms based on the screening measures. Based upon the ADI-R, 14 children qualified for a diagnosis of an ASD, and for 11 of those children a diagnosis of autism was most appropriate. These findings increase our knowledge of developmental disorders associated with the 22q11.2 deletion and point to avenues for future investigation.

Keywords

22q11.2 Deletion; autism; adaptive behavior

Syndromes associated with a microdeletion of chromosome 22q11.2 (e.g., velocardiofacial syndrome, DiGeorge syndrome, conotruncal anomaly face syndrome) represent a relatively commonly identified genetic disorder, with an estimated prevalence of 1 in 4,000 births (Tezenas Du Montcel, Mendizabal, Ayme, Levy, & Philip, 1996). The 22q11.2 deletion underlies several co-occurring physical and cognitive characteristics including cardiac defects, abnormal calcium metabolism, cleft palate/velopharyngeal insufficiency, immunodeficiency, mild mental retardation, language delays, and learning disabilities, though there is considerable inter and intrafamilial variability in the expression of the deletion (McDonald-McGinn *et al*., 1999, 2001). There also appears to be a high incidence of psychiatric and behavioral difficulties in this population. Studies have indicated that disorders such as schizophrenia, mood disorders, and attention deficit hyperactivity disorder are relatively common in individuals with molecularly confirmed 22q11.2 deletion (Arnold, Siegel-Bartelt, Cytrynbaum, Teshima, & Schachar, 2001; Bassett & Chow, 1999).

One of the more ubiquitous behavioral findings in this population has been the prevalence of social skills difficulties (Niklasson, Rasmussen, Oskarsdottir, & Gillberg, 2001,2002;Swillen *et al*., 1999;Woodin *et al*., 2001; for a review of earlier studies see Shprintzen, 2000). Several

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studies report evidence of social skills deficits including withdrawn and shy behaviors, difficulties initiating interactions, and anecdotal evidence of a limited range of facial expressions (Gerdes *et al*., 1999;Niklasson *et al*., 2002;Swillen *et al*., 1999). Despite the evidence that a large percentage of individuals with the 22q11.2 deletion experience psychiatric, social and communication difficulties, there is still a question of whether they qualify for a diagnosis of an autism spectrum disorder (ASD) with greater frequency than the general population. In the present study, we evaluated caregivers' reports of autism spectrum behaviors in a large sample of children with molecularly confirmed 22q11.2 deletion syndrome.

Autism spectrum disorders are atypical developmental delays characterized by impairments in communication, social skills, and restricted or stereotyped patterns of behaviors and interests. A diagnosis within the autism spectrum requires one or more symptoms in each of the three areas of impairment (American Psychiatric Association; Diagnostic and statistical manual of mental disorders; DSM-IV, 1994). The highest functioning individuals qualify for the diagnosis of Asperger's Disorder. This diagnosis is reserved for those with impaired social behavior, including inability to read nonverbal cues, and stereotyped and restricted patterns of interest, but without concomitant delayed language and cognitive ability.

Children diagnosed with an ASD experience marked social impairment characterized by a lack of relatedness and emotionally based connections with other people. For example, they exhibit inappropriate or constricted ranges of facial affect when compared to children without ASDs (Yirmiya, Sigman, Kasari, & Mundy, 1992). Similar behaviors have been described in some studies of individuals with the 22q11.2 deletion (e.g., Roubertie *et al*., 2001), but findings are mixed in terms of the prevalence of autism spectrum symptoms and disorders in this population. Some researchers have reported that the occurrence of ASDs in children with 22q11.2 deletion is relatively uncommon (e.g., Kozma, 1998). Using the Autism Diagnostic Interview to confirm a diagnosis of autism based on strict criteria, one research group reported that none of the 103 autistic children in their sample had a chromosome 22 deletion (Ogilvie, Moore, Daker, Palferman, & Docherty, 2000). Although the Ogilvie *et al*. (2000) sample was drawn entirely from multiplex families, which limits the generalizability of their findings, they concluded that behavioral and psychiatric symptoms observed in the 22q11.2 deletion population were likely inconsistent with autism when using strict criteria for diagnosis.

However, other researchers studying samples of children and adolescents with a molecularly confirmed 22q11.2 deletion have suggested that these individuals exhibit symptoms characteristic of ASDs with far greater frequency than do children without the deletion (Niklasson *et al*., 2001;2002). Using the Asperger Syndrome Screening Questionnaire (Ehlers & Gillberg, 1993), Niklasson and colleagues (2001;2002) reported that 31–35% of children and young adults in their sample of individuals with the 22q11.2 deletion exhibited some "autism spectrum problem." This finding is striking when compared to epidemiological studies that have estimated the prevalence of all ASDs to be approximately 3–6 cases per 1000 (Fombonne, 2003).

Although the variability of findings from past studies is considerable, it is not surprising. Much of the information about the incidence of autism spectrum symptoms and disorders in the 22q11.2 deletion population has been garnered from case studies or studies with small samples (e.g., Kozma, 1998; Niklasson *et al*., 2002). Both the 22q11.2 deletion and disorders within the autism spectrum include a broad range of behavioral patterns, and evolving definitions for ASDs have greatly increased their apparent frequency (Yergin-Allsop *et al*., 2003). Many researchers who have examined behavioral difficulties in individuals with the 22q11.2 deletion have utilized broadband behavior checklists (Swillen *et al*., 1999; Woodin *et al*., 2001), and none have included comprehensive evaluations of autism spectrum behaviors in particular. All

of these issues have rendered determining the prevalence of ASDs among individuals with the 22q11.2 deletion quite difficult.

Given the contradictory findings of diagnostically confirmed prevalence of ASD and several documented descriptions of behaviors that might fall within the autism spectrum, a focused examination of the occurrence of these disorders in individuals with the 22q11.2 deletion syndrome is warranted. In the present study, we examined caregiver reports of developmental milestones and behavioral patterns that characterize ASDs in a relatively large sample of children (2–12 years of age) with a confirmed 22q11.2 deletion in order to determine whether a secondary diagnosis of an ASD would be appropriate.

METHOD

Participants

Participants were 97 caregivers of 98 children (one parent had two children with a 22q11.2 deletion) between the ages of 2 and 12 years involved in a larger study of confirmed 22q11.2 deletions using fluorescence *in situ* hybridization (FISH) at The Children's Hospital of Philadelphia. Caregivers were primarily mothers (88%), and the remaining participants were fathers (11%) or grandparents who were the primary caregivers of the target child (1%). Ninety-two percent of the sample indicated they were married or in a long-term committed domestic partnership. The sample's ethnic composition (91% of caregivers reported ethnicity) was 94% European American. The remaining 6% indicated African American, Latino, or Native American ethnicity. Participating caregivers resided in 28 different states, representing most of the geographic regions of the United States. All parents in the larger genetics study were tested for the 22q11.2 deletion, and none of the parents who participated in the present study had the deletion.

Procedure

All procedures, materials, and forms used in the present study were reviewed and approved by The Children's Hospital of Philadelphia Institutional Review Board. Two hundred fourteen primary caregivers of children who had consent forms filed as part of the larger ongoing study were invited to participate in the present study. Eligible families were sent a packet containing a cover letter explaining that researchers were initiating an additional study to gather information about the different types of behaviors exhibited by children with the 22q11.2 deletion. The packet included an autism screening measure (depending on the age of the child, either the Modified Checklist for Autism in Toddlers or the Social Communication Questionnaire), the consent form, and a self-addressed, stamped return envelope. If they desired to participate in the present study, caregivers were requested to read and sign the consent form, complete the screening measure, and return the packet to the Children's Hospital of Philadelphia. They were also advised that a trained interviewer would be calling their home to speak with them about a wide range of behaviors exhibited by their child with the 22q11.2 deletion.

Of the 214 packets sent, 23 were returned undeliverable, indicating that the family had moved and the forwarding period had expired. After one month, 71 caregivers completed and returned packets. The 120 caregivers who had not yet responded were called on the telephone and asked if they were interested in participating in the study. Four individuals indicated that they did not wish to participate, and seven of the telephone numbers were disconnected. A second wave of study packets was then sent to the remaining 109 caregivers. Thirty additional caregivers subsequently returned study packets. Six caregivers returned completed measures but did not return the signed consent forms. These individuals were contacted by telephone and sent another cover letter and consent form, informing them that their information could not be used

unless they returned the signed consent form indicating their understanding of all aspects of the present study. Two of these caregivers returned signed consent forms, and the remaining four who did not were not included in the study. Therefore, the participation rate was 45.3%. Excluding individuals who were inaccessible due to changes of address or phone number (n = 30), the adjusted participation rate was 55.4%.

Caregivers who returned signed consent forms and screening measures were contacted by telephone at a time and telephone number they had indicated was convenient. A trained interviewer administered the Vineland Adaptive Behavior Scales—Interview Edition over the telephone. Typically, 3–4 attempts were required to reach caregivers in order to administer the Vineland. Telephone administration required 15–45 minutes, depending on the age of the child. Of the 97 participating caregivers, 93 completed the telephone interview. Four caregivers could not be reached after 10 attempts and did not complete the Vineland.

After the Vineland had been administered, caregivers who had rated their children above the cut-off score on the autism screening measure or who had indicated their children had been previously diagnosed with an ASD were invited to participate in an additional interview (the Autism Diagnostic Interview—Revised), to be scheduled at a time of their choosing. Typically, 5–6 attempts were required to schedule the ADI-R interview, but in all but one case, the interview was completed over the course of one 1–2 hours telephone call. All but one of the parents whose child met these criteria completed the Vineland interview and agreed to participate in the ADI-R. However, after beginning to participate in the ADI-R telephone interview, one caregiver indicated that she could not continue due to time and memory constraints. She was thanked for her time and the information she had provided up to that point on the ADI-R was not used in analyses. Parents who completed the ADI-R and whose children met criteria for an ASD were contacted by telephone and given oral and written feedback. All caregivers who participated in the present study received a written summary of the results of the study.

Measures

Autism Spectrum Behaviors and Symptoms—In order to assess behaviors and symptoms that are characteristic of ASDs, caregivers completed a measure that screens for these behaviors. Caregivers of children ages four years and older (n = 78) completed the Social Communication Questionnaire, Lifetime Version (SCQ, previously known as the Autism Screening Questionnaire; Berument, Rutter, Lord, Pickles, & Bailey, 1999), a 40-item scale that has shown good discriminant validity between children with and without pervasive developmental disorders. Items 20–40 of the Lifetime version focus on the 12 months between the child's fourth and fifth birthdays. Examples of items include, "Has she/he ever got her/his pronouns the wrong way round (i.e. saying 'you' or 'she/he' for 'I'?)," "Has she/he ever seemed to be more interested in parts of a toy or an object (e.g., spinning the wheels of a car), rather than using the object as it was intended?," and "When she/he was 4-to-5, did she/he usually look at you directly in the face when doing things with you or talking with you?." Items are scored in yes–no format and several items are reverse scored. Higher scores indicate higher numbers of autism spectrum symptoms and behaviors, and a cut-off score of 15 represents the best discrimination between children with and without ASDs.

The Modified Checklist for Autism in Toddlers (M-CHAT; Robins, Fein, Barton, & Green, 2001) was completed by caregivers of children between the ages of 24 and 48 months (n = 20). The M-CHAT is a 23-item measure designed to detect disorders on the autism spectrum in very young children. Examples of items include, "Does your child ever use his/her pointer finger to point, to show interest in something?," "Does your child imitate you (e.g., you make a face—will your child imitate it)?," and "Does your child make unusual finger movements

near his/her face?" A score of 3 of the 23 items or 2 of 6 "critical" items has been shown to discriminate between children who have an ASD and those who do not.

All caregivers were asked an additional question regarding whether their child had been diagnosed with any ASD. If children's scores on the screening measure exceeded the established cut-off score, or if caregivers reported that their child had been already diagnosed with an ASD, the 2000 version of the Autism Diagnostic Interview—Revised (ADI-R; Rutter, Le Conteur, & Lord, 2003, unpublished at time of administration in the present study) was administered through a telephone interview. The ADI-R is a standardized, semi-structured, investigator-based interview for primary caregivers of children and adults for whom autism or pervasive developmental disorder is a possible diagnosis. A trained, reliable interviewer (in the present study, AW) assesses caregivers' behavioral descriptions and responses to questions addressing early development, communication, social behavior and play, interests, and general behaviors that are associated with ASDs (Lord, 1995). Items are coded and converted to numerical scores for the domains of reciprocal social interaction, communication, and repetitive behaviors, stereotyped patterns on a diagnostic algorithm for the DSM-IV and ICD-10 criteria for autism and pervasive developmental disorder (Lord, Rutter, & LeConteur, 1994; Sæmundsen Magnusson, Smari, & Sigurdottir, 2003). A research diagnosis of autism is given to children who meet ICD-10/DSM-IV diagnostic criteria in each of the three content areas, and who are exhibiting some abnormality in at least one area by 36 months of age, as described by the caregiver or judged by the interviewer (Lord *et al*., 1994). Children meeting two of the three content areas are given a research diagnosis of autism spectrum disorder ("spectrum" cases).

Adaptive Behavior—The Vineland Adaptive Behavior Scales—Interview Edition, Survey Form is a nationally normed measure that yields standard scores for children's adaptive behaviors in the following domains: (a) Socialization, encompassing a child's interpersonal, play and leisure activities, and coping skills; (b) Daily Living Skills, encompassing a child's self-care, domestic, and community skills; (c) Communication, encompassing a child's receptive, expressive, and writing skills, and (d) Motor, encompassing fine and gross motor skills. The Survey form of this measure is a semi-structured interview conducted with the child's primary caregiver by a trained interviewer. Scores for each item are determined by the interviewer after the caregiver describes how the child performs each activity specified and provides examples. An Adaptive Behavior Composite was determined from the sums of the domain standard scores. The Vineland measure is commonly used with special needs populations (Gillham, *et al*., 2000).

RESULTS

Refer to Table I for means and standard deviations for all measures used in the study. Children ranged in age from 22 to 153 months, and 57% were male. On average, caregivers indicated that their children were experiencing mild global developmental delays based on the Vineland Adaptive Behavior Scales Composite standard score (M = 70.02, SD = 18.79).

Of the 78 children whose caregivers completed the SCQ, 8 had been previously diagnosed with an ASD (7 were male). A total of 15 children received scores above the cut-off on the SCQ. Six of the previously diagnosed children received scores above the cut-off (the other two received scores 2–3 points below the cut-off). Therefore, 17 of these children met criteria for their caregivers to complete the ADI-R (76% male).

None of the 20 children whose caregivers completed the M-CHAT had been previously diagnosed with an ASD. All of the five children whose scores exceeded the cut-off on the M-CHAT were male. Taken together, 22 children met criteria for their caregivers to receive the

ADI-R, and 20 of those caregivers completed this interview. Seventy-six percent of the children whose caregivers completed the ADI-R received Vineland Composite scores in the significantly delayed range (a score of 69 or below), compared with 44% of children who did not meet criteria for the ADI-R. Table I presents means and standard deviations of all variables separately for children who did and did not meet criteria for caregivers to complete the ADI-R.

Of the 20 children whose caregivers completed the ADI-R, 11 were reportedly exhibiting behaviors that exceeded the cut-off points in all three domains of behavior (communication, social relatedness, and repetitive or stereotyped patterns of behavior), which qualified them for a research diagnosis of autism. This number of children represents approximately 11% of the total sample. An additional three children were rated as exceeding the cut-off points in two content domains, indicating that they met criteria for an ASD. Therefore, the total number of children who qualified for a diagnosis of an ASD represents approximately 14% of the total sample.

Children qualifying for a diagnosis of ASD in this sample ranged in age from 3.24 to 11.53 years, and 85.7% were male. Table II presents summary characteristics of children whose caregivers completed the ADI-R. It is interesting to note that over half (n = 8) of the children who met criteria for an ASD based on the ADI-R had not been previously diagnosed.

DISCUSSION

Findings from this study support some past research suggesting that children with the 22q11.2 deletion syndrome may exhibit ASDs at a markedly higher rate than that found in the general population. However, although a diagnosis of an ASD was appropriate for approximately 14% of the sample, this proportion represents a substantially lower number than previously suggested (Niklasson *et al*., 2001). The explanation for this discrepancy becomes clear when taking the methods of these studies into account. The present study used strict diagnostic criteria for the purpose of screening and classifying children as exhibiting levels of symptoms commensurate to what one might observe in a child with an ASD. Although previous studies also used screening measures, the present study included a more in-depth diagnostic interview to further explore children's symptoms. Use of these stringent criteria determined that several children whose caregivers had indicated were exhibiting significant levels of autism spectrum symptoms did not meet requirements to receive a diagnosis of an ASD.

Even when applying the strict diagnostic criteria by administering the ADI-R, the findings of the present study appear to conflict with those of Ogilvie *et al.* (2000), who reported that none of the children with autism in their large sample of individuals from multiplex families exhibited a deletion on chromosome 22. There are some possible explanations for the discrepancies in these findings. First, we used the ADI-R (2003, unpublished at time of administration) version of the diagnostic interview, which was revised from the previous versions to improve differentiation between autism and other developmental disorders such as fragile X, particularly in younger children. The revision was also intended to better distinguish between delays in development and developmental deviance, which was important in the current study because of the prevalence of developmental delays. The differences between the ADI (the algorithm from which Ogilvie and colleagues used to confirm a diagnosis of autism in their sample) and the revision may have enabled us to detect autism symptoms in a sample of children already identified as having special needs. Furthermore, Ogilvie and colleagues determined the occurrence of the 22q11.2 deletion in a unique sample of children with autism, limiting their investigation to only individuals from multiplex families. This constraint limits the generalizability of their findings, as multiplex cases of autism may represent a specific genetic subgroup unto themselves. Finally, the 22q11.2 deletion occurs less frequently in the

general population than does autism, and thus the Ogilvie *et al*. (2000) study may not have had sufficient power to accurately estimate the prevalence of the 22q11.2 deletion in individuals with autism. Although additional studies are required to replicate the findings of the present study, it does appear as if autism spectrum disorders occur more frequently in the population of children with the 22q11.2 deletion than in the general population.

Characteristics of children in the sample who met criteria for autism based on their caregivers' reports were similar to those reported in the general population of individuals with ASDs. Even when taking into account the disproportionate percentage of males in the sample, the male-female ratio in children who met criteria for autism was 3–4:1, which is consistent with past research (Burd, Severud, Kerbeshian, & Klug, 1999; Fombonne, 1999, 2003; Steffenburg & Gillberg, 1986). In addition, although the sample in general tended to be mildly globally developmentally delayed, children who met criteria for ASD tended to have more severe delays, which is in line with past research that has suggested that ASD is often co-morbid with severe to profound cognitive impairments (Fombonne, 1999, 2003; Gillberg *et al*., 1990; Lord & Volkar, 2002; Sigman & Capps, 1997).

Reports from caregivers in the present study suggest that perhaps many children who have the 22q11.2 deletion and are exhibiting symptoms of ASDs may not be formally diagnosed with autism. There are several explanations for the possible under-identification of ASDs in this population. The 22q11.2 deletion is often identified at birth, making caregivers immediately aware that their child may not develop typically. Therefore, caregivers may notice unusual or atypical behaviors as their children develop, but they may integrate these behaviors into their conceptualization of the genetic disorder and be less likely to question them than parents of children who were not identified at birth as having a special condition. Anecdotally, some caregivers in the study who completed the ADI-R attributed their children's behaviors directly to the 22q11.2 deletion rather than to another distinct psychiatric or developmental disorder. Additionally, because of the lack of general knowledge about individuals with the 22q11.2 deletion, many of their caregivers are placed in the unfortunate position of having to educate and inform the professionals who are working with them. Professionals observing and evaluating these children may also integrate autism spectrum-like behaviors into a broader conceptualization of the 22q11.2 deletion rather than identifying them as fitting into a particular diagnostic category.

Another explanation for the under-identification of ASDs in children with the 22q11.2 deletion is that medical procedures and hospital stays in early childhood (which these children often experience) may further obscure caregivers' perspectives of their children's behaviors and abilities. For example, losses of skills or regressions in one area of development, common to children with ASDs, were sometimes explained by caregivers in the present study as the result of long and trying hospitalizations. Surgical procedures could also obscure possible delays in language and social responsiveness. Aggressive behaviors may be dismissed by parents who have been close observers of their child's hardships and who perceive such behavior solely as frustration due to physical inability to speak or ambulate. Finally, in the context of stressful medical care, particularly early in life, symptoms of ASDs may be de-prioritized when caregivers, who are simply thankful that their child is surviving, discuss issues with professionals.

Limitations

One weakness of the present study is method variance. Due to the nature of the sample, which included families residing in several different geographical regions throughout the United States, direct observation of the children at The Children's Hospital of Philadelphia during the time frame of the present study was not feasible. Therefore, evaluation was conducted via mail survey and telephone interviews with the caregivers of these children. We attempted to mitigate

potential reporter bias by using some measures that were scored by a trained interviewer rather than caregivers themselves. Although this type of interview measure is still influenced by caregiver reports, the number value assigned to a particular behavior is based on concrete descriptions coded by a trained interviewer rather than subjective impressions. Despite use of these measures, however, the results should be interpreted in light of the fact that caregivers provided all of the information.

Another potential limitation of the present study is the use of the ADI-R to detect ASD within this sample of children with an established genetic diagnosis. The ADI-R has been revised to discriminate ASD from other genetic disorders (e.g., Fragile X). It is possible, however, that the estimated prevalence of ASD in this sample of children with 22q11.2 deletion may have been somewhat inflated due to a measurement artifact. That is, the ADI-R may not be able to reliably discriminate behaviors that characterize children with ASD from behaviors of children with 22q11.2 deletion. This potential weakness in the ADI-R, which certainly applies to other measures such as the Vineland Adaptive Behavior Scales, highlights the importance of using multiple methods to carefully and thoroughly assess ASD, particularly in children who have genetic diagnoses.

Certain characteristics of the sample may limit the generalizability of these findings. There is a possibility of ascertainment bias, in that all children described in the present study had experienced manifestations of the 22q11.2 deletion that were apparent enough to warrant genetic testing. This characteristic suggests that they may have been more seriously affected than other children who have the deletion but have not experienced the structural anomalies such as congenital heart defects or the other health problems such as hypocalcemia associated with the deletion. It is also possible that parents of children who were more seriously affected by the 22q11.2 deletion were more motivated to respond to the invitation to participate than parents of children with fewer difficulties. As a result, the findings may represent an overestimate of the prevalence of ASD in the population of children with 22q11.2 deletion. Moreover, participating families had the time and resources to allow their children to travel to The Children's Hospital of Philadelphia, in some cases from considerable distances, to participate in the larger study. They were further able to take the time to participate in the current study over the telephone, which may mean that they represented a slightly more economically privileged group. Given these sample characteristics, findings should be interpreted with caution, as this sample may not be fully representative of all individuals with the 22q11.2 chromosomal deletion.

Implications and Future Directions

This study represents one of the initial steps in determining the prevalence of ASDs in individuals with the 22q11.2 deletion. Future studies should employ direct observation measures, such as the Autism Diagnostic Observation Schedule (ADOS; Lord *et al.*, 2000), to evaluate these children for symptoms of autism. Although it would be difficult to include a geographically diverse sample, a secondary study might utilize a face-to-face administration of the ADI-R. A replication of the results would not only support the findings, but would also support the use of the ADI-R through telephone administration. Replication would broaden the scope of this tool and its availability for broad-based studies by supporting its use through a telephone interview, rather than requiring a face to face interview. Others have already presented findings supporting this method of administration with a screening version of the ADI-R (Vrancic *et al*., 2002).

Diagnosis is crucial to our understanding of disease. Through this investigation and future ones, we are obtaining a broader understanding of the very meaning of autism and the 22q11.2 deletion syndrome. Such research provides better understanding of co-morbid conditions and fleshes out our understanding of the genetic components of these disorders. Future research

must continue to relate overlapping disorders while simultaneously providing more definitive definitions of ASDs. Possibly, ASDs overlap with other disorders, such as the 22q11.2 deletion, in only a few specific subgroups. Subsequent studies should explore this possibility in order to increase our knowledge of potential genetic subtypes of autism (Bassett & Chow, 1999; cf. Ogilvie *et al.*, 2000). Further research focusing on linkages between specific genes and ASDs is greatly needed, as phenotype research on family characteristics and personality types remains imprecise and relies upon clinical interviews that require further testing and standardization (e.g., M-PAS, FHI; Bolton *et al.*, 1994; Folstein *et al.*, 1999; Piven, Palmer, Jacobi, Childress, & Arndt, 1997; Szatmari *et al.*, 1995, 2000).

Findings from the present study may directly impact current practices and medical care for children with a 22q11.2 deletion. In this study, hospital stays and previous diagnoses might have delayed the detection of ASDs. Parents may not be have been prepared to recognize behaviors that did not confirm the primary diagnosis or may have ignored these behaviors as the result of the trauma of their child's hospitalization. These factors suggest that certain situations, such as prematurity or regular hospital stays, require careful attention and consideration of missed diagnoses. Future studies should investigate methods to prevent biased interpretations of symptoms in the context of the 22q11.2 deletion. In addition, it might be fruitful to provide all children with a 22q11.2 deletion with more stringent developmental assessments that specifically rule out or confirm ASDs.

Given the host of difficulties faced by many children with a 22q11.2 deletion, such as chronic medical conditions, learning disabilities, and other psychiatric issues, some may question the incremental value to families of formally diagnosing an ASD. However, the existence of empirically supported treatments and interventions for individuals with autism means that children who are diagnosed can have access to early intervention and ongoing special services that can improve social, behavioral, and language functioning (Goldstein, 2002; Horner, Carr, Strain, Todd, & Reed, 2002; McConnell, 2002). Diagnosis provides understanding to parents and informs their attributions about their children's behaviors. Rather than treat behaviors related to the ASD as naughty, parents can find therapeutic ways to mitigate behavioral difficulties. In addition, diagnosis prepares parents for areas of difficulty that develop in the later years of autism, including depression among higher functioning individuals (Ghaziuddin, Ghaziuddin, & Greden, 2002; Volkmar *et al.*, 1999) and the need for residential living and preparation for sheltered occupations (Frith, 1991). An accurate diagnosis of ASD may expedite acquisition of services and be particularly empowering for families of children with a 22q11.2 deletion, who are too often faced with informing medical and educational professionals about this little known but relatively common genetic disorder, about which we still have so much to learn.

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Table I

Total Sample Raw Score Means and Standard Deviations for All Variables. Raw Score Means and Standard Deviations for All Variables for (a) Children Who Met Criteria for ADI-R, and (b) Children Who Did Not Meet Criteria for ADI-R

Variable	M	SD	n
Child age (in years)	6.36	2.71	98
Vineland Composite Standard Score	70.02	18.79	94
Vineland Communication Domain	74.48	20.39	94
Vineland Daily Living Skills Domain	65.30	20.23	94
Vineland Socialization Domain	83.26	16.15	94
SCQ	9.47	6.45	78
M-CHAT	1.45	1.28	20
(a)			
Child age (in years)	6.89	3.01	22
Vineland Composite Standard Score	54.90	16.88	21
Vineland Communication Domain	59.19	18.98	21
Vineland Daily Living Skills Domain	49.38	21.41	21
Vineland Socialization Domain	69.86	16.10	21
SCQ	19.35	4.12	17
M-CHAT	3.2	.45	5
(b)			
Child age (in years)	6.21	3.01	76
Vineland Composite Standard Score	74.37	17.06	73
Vineland Communication Domain	78.88	18.69	73
Vineland Daily Living Skills Domain	69.88	17.50	73
Vineland Socialization Domain	87.12	14.05	73
SCQ	6.72	3.68	61
M-CHAT	.87	.83	15

Table II

Descriptive Characteristics of Children Whose Caregivers Completed the ADI-R

		SCQ	SCQ	Vineland Composite	Vineland Composite	Prev. Dx'd?
	n	M	SD	M	SD	n
Did not meet criteria for ASD	6	15.67	2.52	67.50	17.80	1
Met criteria for ASD	14	20.00	4.14	51.14	13.69	6